مجلــة الشمـال

للعلـــوم

الأساسية والتطبيقية

دورية علمية محكمة

مجلة الشمال للعلوم الأساسية والتطبيقية (JNBAS)

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المملكة العربية السعودية

مجلة الشمال للعلوم الأساسية والتطبيقية (JNBAS)

التعريف بالمجلة

تعنى المجلة بنشر البحوث والدراسات العلمية الأصيلة في مجال العلوم الأساسية والتطبيقية، باللغتين العربية والإنجليزية، كما تهتم بنشر جميع ما له علاقة بعرض الكتب ومراجعتها أو ترجمتها، وملخصات الرسائل العلمية، وتقارير المؤتمرات والندوات العلمية، وتصدر مرتين في السنة (مايو ـ نوفمبر).

الرؤية

الريادة في نشر البحوث العلمية المحكمة، وتصنيف المجلة ضمن أشهر الدوريات العلمية العالمية.

الرسالة

نشر البحوث العلمية المحكمة في مجال العلوم الأساسية والتطبيقية وفق معايير عالمية متميزة.

أهداف المجلة

1) أن تكون المجلة مرجعًا علميًا للباحثين في العلوم الأساسية والتطبيقية.
2) تلبية حاجة الباحثين إلى نشر بحوثهم العلمية، وإبراز مجهوداتهم البحثية على المستويات المحلية والإقليمية والعالمية.
3) المشاركة في بناء مجتمع المعرفة بنشر البحوث الرصينة التي تؤدي إلى تنمية المجتمع.
4) تغطية أعمال المؤتمرات العلمية المحكمة.

شروط قبول البحث

1) الأصالة والابتكار وسلامة المنهج والاتجاه.
2) الالتزام بالمناهج والأدوات والوسائل العلمية المتبعة في مجاله.
3) الدقة في التوثيق والمصادر والمراجع والتخريج.
4) سلامة اللغة.
5) أن يكون غير منشور أو مقدم للنشر في أي مكان آخر.
6) أن يكون البحث المستل من الرسائل العلمية غير منشور أو مقدم للنشر، وأن يشير الباحث إلى أنه مستلٌّ.

شروط النشر

أولاً: ضوابط النص المقدم للنشر

1) ألا تزيد صفحاته عن (35) صفحة من القطع العادي (A4).

2) أن يحتوي على عنوان البحث وملخص باللغتين العربية والإنجليزية في صفحة واحدة، بحيث لا يزيد عن (250) كلمة للملخص الأصيل، وأن يتضمن البحث كلمات مفتاحيةٍ دالةٍ على التخصص الدقيقِ للبحثِ باللغتين، بحيث لا يتجاوز عددها (6) كلمات توضع بعد نهاية كل ملخص.

3) أن يذكر اسم المؤلف وجهة عمله بعد عنوان البحث مباشرة باللغتين العربية والإنجليزية.

4) أن تقدم البحوث العربية مطبوعة بخط (Simplified Arabic)، بحجم (14) للنصوص في المتن، وبالخط نفسه بحجم (12) للهوامش.

5) أن تقدم البحوث الإنجليزية مطبوعة بخط (Times New Roman) بحجم (12) للنصوص في المتن، وبالخط نفسه بحجم (9) للهوامش.

6) كتابة البحث على وجه واحد من الصفحة، مع ترك مسافة سطر واحد بين السطور، وتكون الحواشي 2.5 سم على الجوانب الأربعة للصفحة، بما يعادل 1.00 إنش (بوصة).

7) التزام الترتيب الموضوعي الآتي:

المقدمــة: تكون دالة على موضوع البحث، والهدف منه، ومنسجمة مع ما يَرِدُ في البحث من معلومات وأفكار وحقائق علمية، كما تشير باختصار إلى مشكلة البحث، وأهمية الدراسات السابقة.

العرض: يتضمن التفاصيل الأساسية لمنهجية البحث، والأدوات والطرق التي تخدم الهدف، وترتب المعلومات حسب أولويتها.

النتائج والمناقشة: يجب أن تكون واضحة موجزة، مع بيان دلالاتها دون تكرار.

الخاتمة: تتضمن تلخيصًا موجزًا للموضوع، وما توصل إليه من نتائج، مع ذكرِ التوصيات والمقترحات.

8) أن تدرج الرسوم البيانية والأشكال التوضيحية في النص، وترقم ترقيماً متسلسلاً، وتكتب أسماؤها والملاحظات التوضيحية أسفلها.

9) أن تدرج الجداول في النص، وترقم ترقيماً متسلسلاً، وتكتب أسماؤها أعلاها، وأما الملاحظات التوضيحية فتكتب أسفل الجدول.

10) ألا توضع الهوامش أسفل الصفحة إلا عند الضرورة فقط، ويشار إليها برقم أو نجمة، ويكون الخط فيها بحجم (12) للعربي و (9) للإنجليزي.

11) لا تنشر المجلة أدوات البحث والقياس، وتقوم بحذفها عند طباعة المجلة.

12) أن يُراعى في منهج توثيق المصـادر والمراجـع داخل النص نظام (APA)، وهـو نظام يعتمـد ذكر الاسم والتاريخ (name/year) داخل المتن، ولا يقبل نظام ترقيم المراجع داخل النص مع وضع الحاشية أسفل الصفحة، وتوضع المصادر والمراجع داخل المتن بين قوسين حسب الأمثلة الآتية: يذكر اسم عائلة المؤلف متبوعا بفاصلة، فسنة النشر، مثلا: (مجاهد، 1988م). وفي حالة الاقتباس المباشر يضاف رقم الصفحة مباشرة بعد تاريخ النشـر مثلا: (خيري، 1985م، ص:33). أما إذا كان للمصدر مؤلفان فيذكران مع اتباع الخطوات السابقة مثلا: (الفالح وعياش، 1424هـ). وفي حالة وجود أكثر من مؤلفين فتذكر أسماء عوائلهم أول مرة، مثلا: (مجاهد والعودات والشيخ، 1408هـ)، وإذا تكرر الاقتباس من المصدر نفسه فيشار إلى اسم عائلة المؤلف الأول فقط، ويكتب بعده وآخرون مثل: (مجاهد وآخرون، 1408هـ)، على أن تكتب معلومات النشر كاملة في قائمة المصادر والمراجع.

13) تخرج الأحاديث والآثار على النحو الآتي:

(صحيح البخاري، ج:1، ص: 5، رقم الحديث 511).

14) توضع قائمة المصادر والمراجع في نهاية البحث مرتبة ترتيباً هجائياً حسب اسم العائلة، ووفق نظام جمعية علم النفس الأمريكية (APA) الإصدار السادس، وبحجم (12) للعربي و(9) للإنجليزي، وترتب البيانات الببليوغرافية على النحو الآتي:

- **الاقتباس من كتاب لمؤلف واحد:**

الخوجلي، أحمد. (2004م). *مبادئ فيزياء الجوامد*. الخرطوم، السودان: عزة للنشر والتوزيع.

- **الاقتباس من كتاب لأكثر من مؤلف:**

نيوباي، تيموثي، وستيبتش، دونالد، وراس، جيمس. (1434هـ/2013م). *التقنية التعليمية للتعليم والتعلم*. الرياض، المملكة العربية السعودية: دار جامعة الملك سعود للنشر.

- **الاقتباس من دورية:**

النافع، عبداللطيف حمود. (1427هـ). أثر قيادة السيارات خارج الطرق المعبدة في الغطاء النباتي بالمنتزهات البرية: دراسة في حماية البيئة، في وسط المملكة العربية السعودية. *المجلة السعودية في علوم الحياة*، *14*(1)، 53-72.

- **الاقتباس من رسالة ماجستير أو دكتوراه:**

القاضي، إيمان عبدالله. (1429هـ). *النباتات الطبيعية للبيئة الساحلية بين رأسي تنورة والملوح بالمنطقة الشرقية: دراسة في الجغرافيا النباتية وحماية البيئة*. رسالة دكتوراه غير منشورة، كلية الآداب للبنات، الدمام، المملكة العربية السعودية: جامعة الملك فيصل.

- **الاقتباس من الشبكة العنكبوتية (الإنترنت):**

- الاقتباس من كتاب:

المزروعــــي، م.ر. و المدنـي، م.ف. (2010م). *تقييــم الأداء فـي مؤسســات التعليــم العالـي*. المعـرِّف الرقمـي (DOI:10.xxxx/xxxx-xxxxxxxx-x)، أو برتوكـول نقـل النصــوص التشـعبي (...http://www)، أو الرقـم المعيــاري الدولـي للكتاب (ISBN: 000-0- 00 - 000000-0)

– الاقتباس من مقالة في دورية:

المدني، م.ف. (2014). مفهوم الحـوار في تقريب وجهات النظر. *المجلة البريطانية لتكنولوجيا التعليم*، *11*(6) 225-260، المعرِّف الرقمـي (DOI:10.xxxx/xxxx-xxxxxxxx-x) أو برتوكول نقل النصوص التشعبي (http://onlinelibrary.wiley.com/journal/10.1111)، أو الرقم المعياري التسلسلي الدولي للمجلة (ISSN: 8535 - 1467).

(15) يلتزم الباحث بترجمة (أو رومنة) أسماء المصادر والمراجع العربية إلى اللغة الإنجليزية في قائمة المصادر والمراجع. وعلى سبيل المثال:

الجبر، سليمان. (1991م). تقويم طرق تدريس الجغرافيا ومدى اختلافها باختلاف خبرات المدرسين وجنسياتهم وتخصصاتهم في المرحلة المتوسطة بالمملكة العربية السعودية. *مجلة جامعة الملك سعود- العلوم التربوية*، *3*(1)، 143-170.

Al-Gabr, S. (1991). The Evaluation of Geography Instruction and the Variety of its Teaching Concerning the Experience, Nationality, and the Field of Study in Intermediate Schools in Saudi Arabia *(in Arabic)*. *Journal of King Saud University- Educational Sciences*, *3*(1), 143-170.

(16) تستخدم الأرقام العربية الأصلية (0، 1، 2، 3، ...) في البحث.

ثانياً: الأشياء المطلوب تسليمها

1) نسخة إلكترونية من البحث بصيغتي (WORD) و (PDF)، وترسلان على البريد الإلكتروني الآتي:

s.journal@nbu.edu.sa & s.journal.nbu@gmail.com

2) السيرة الذاتية للباحث، متضمنة اسمه باللغتين العربية والإنجليزية، وعنوان عمله الحالي، ورتبته العلمية.

3) تعبئة النماذج الآتية:
   أ - نموذج طلب نشر بحث في المجلة.
   ب - نموذج تعهد بأن البحث غير منشور أو مقدم للنشر في مكان آخر.

ثالثاً: تنبيهات عامة

1) أصول البحث التي تصل إلى المجلة لا تردّ سواء أَنُشِرَتْ أَم لم تنشر.

2) الآراء الواردة في البحوث المنشورة تعبر عن وجهة نظر أصحابها.

3) تؤول جميع حقوق النشر للمجلة في حال إرسال البحث للتحكيم وقبوله للنشر.

المحتويات

الأبحاث العربية

الأبحاث الإنجليزية

الأبحاث باللغة العربية

تطبيــق نمــوذج SLEUTH الرقمـي لقيــاس اتجاهــات النمـو الحضــري لمدينـة الخرطــوم الكبــرى ـ السـودان

طارق محمد سليمان[1]*

ملخص البحث: هدفت الدراسة الى التعرف على أهم العوامل المؤثرة في تحديد اتجاهات النمو الحضري في مدينة الخرطوم الكبرى، واستعراض وتحليل سياسات التخطيط الحضري السابقة من خلال دراسة تفصيلية للمخططات الهيكلية التي تم تطبيقها من قبل، والأسس التي قامت عليها، والتغيرات التي طرأت أثناء عملية تنفيذها. ومن ثم تقييم الوضع الراهن مع نمذجة للاتجاهات المستقبلية للنمو الحضري. استخدمت الدراسة كلا من المنهج الوصفي والمنهج الاستقرائي، كما عملت على تحليل البيانات باستخدام أدوات التحليل المكاني التي توفرها برمجيات نظم المعلومات الجغرافية، وتم وضع نموذج لاتجاهات النمو الحضري المستقبلي في مدينة الخرطوم الكبرى حتى العام 2033م مستخدماً نموذج SLEUTH لقياس اتجاهات النمو الحضري، مستصحباً عند تطبيق النموذج مخرجات المخطط الهيكلي لولاية الخرطوم (2008 - 2033م). خرجت الدراسة بعدد من النتائج من أهمها: أنه إذا استمرت معدلات النمو الحضري لمدينة الخرطوم بنفس الاشتراطات الحالية سوف يتمدد النمو الحضري ليشمل مناطق خارج نطاق الطريق الدائري والذي تم تحديده كحد للنمو الحضري المستقبلي للمدينة. وقد أوصت الدراسة بضرورة تحديث المخطط الهيكلي لولاية الخرطوم وتنقيحه على أسس علمية تراعي المتغيرات البشرية والمستجدات التخطيطية والتنموية للسودان ككل، وولاية الخرطوم على وجه الخصوص.

الكلمات المفتاحية: التحليل المكاني؛ النمو الحضري؛ النمذجة؛ الخرطوم الكبرى.

* للمراسلة:

(1) قسم الأمـن الإنسـاني، كليـة العلـوم الإسـتراتيجية، جامعـة نايـف العربيـة للعلـوم الأمنيـة، الريـاض، الرمـز البريـدي 11452، ص.ب. 6830، المملكـة العربيـة السـعودية.

e-mail: dr.tarigmoh@nauss.edu.sa

APPLICATION OF THE DIGITAL SLEUTH MODEL TO MEASURE THE URBAN GROWTH TRENDS OF GREAT KHARTOUM - SUDAN

Tarig Mohamed Suliman[1]*

Abstract: The study aimed to identify the most important factors affecting the identification of urban growth trends in Great Khartoum and to review and analyze the previous urban planning policies through a detailed study of the structural plans that were applied previously, the bases on which they were based, and the changes that occurred during the implementation process. At the end, an assessment of the current situation with modeling the future trends of urban growth was implemented. The study used both the descriptive and the inductive methods. It also analyzed the data using spatial analysis tools provided by GIS software. A model of future urban growth trends was developed in great Khartoum City until 2033 using the SLEUTH model for measuring urban growth trends, as well as outputs of Khartoum State structural chart when applying the model (2008-2033). The study come out with a number of results, the most important of which is that if urban growth rates of Khartoum City continue with the same current conditions, urban growth will be extended to areas outside the ring road, which is set as the limit for future urban growth of the city. The study recommended the need to update the structural chart of the state of Khartoum and revise it on scientific grounds, taking into account the human changes and the planning developments of Sudan as a whole and the state of Khartoum in particular.

Keywords: Spatial analysis; Urban growth; Modeling; Great Khartoum.

* **Corresponding Author**:

(1) Department of Human Security, Faculty of Strategic Sciences, Naif Arab University for Security Sciences, Riyadh, Postal Code 11452, P.O. Box 6830, Kingdom of Saudi Arabia.

e-mail: dr.tarigmoh@nauss.edu.sa

1. المقدمـــة

هنالك شبه اتفاق بين الجغرافيين والمختصين في تخطيط المـدن علـى أن جميـع المسـتوطنات البشـرية (حضريـة أو ريفيـة) تنمـو وتتوسـع باتجاهـات مختلفـة لاستيعاب الزيـادة السـكانية والوظيفيـة فيهـا، وأن عمليـة النمـو والامتـداد الحضـري لـم تكـن وليـدة الصدفـة وإنمـا تكمـن وراءهـا أسـباب طبيعيـة وبشـرية (اجتماعيـة وسياسـية واقتصاديـة)، إلا أن معرفـة دور كل سـبب مـن هـذه الأسـباب وآليـة عملهـا فـي رسـم صـورة النمـو والامتـداد الحضـري لتلـك المسـتوطنات يتبايـن تبعـاً للمسـتوطنة البشـرية ومحيطهـا.

ترتبـط عمليـات تخطيـط وتطويـر المـدن بموجهـات وقوانين حسـب السياسـات المتبعـة فـي هـذا المجـال، حيـث كانـت تعتمـد مـع بدايـات القـرن العشـرين الخطـط الشـاملة وهـي خطـط تركـز الجانـب المـادي الفيزيقي وتوظيفه فـي مجـال التخطيـط الحضـري، ومـن خـلال الممارسـة اقتنـع المخططـون بقصـور الخطـط الشـاملة لأنهـا لا تتماشـى مـع التغيـرات الحضريـة السـريعة فـكان ذلـك سـبباً فـي إهمالهـا واستعيض عنهـا بالخطـط الهيكليـة فـي نهايـة القـرن العشـرين، ثـم تـم الاسـتعاضة عنهـا بالتخطيـط الاسـتراتيجي المكانـي فـي الآونـة الأخيـرة. وتحتـاج جميـع الموجهـات إلـي أدوات معلوماتيـة وتخطيطيـة وإداريـة وتنفيذيـة فاعلـة للتعامـل مـع النظـام الحضـري المعقـد والمتغيـر باسـتمرار. كل ذلـك يحتـم ضـرورة بنـاء نظـام تقنـي فاعـل ومتكامـل للمعلومـات الحضـرية (Urban Information System). ويمكـن اسـتخدام نظـم المعلومـات الجغرافيـة بكفـاءة عاليـة فـي بنـاء وتشـغيل هـذا النظـام.

تعـد الخرطـوم الكبـرى مدينـة مترّاميـة الأطـراف وسـريعة النمـو مـن جـراء التجمعـات الريفيـة التـي تحيـط بهـا، وذات جاذبيـة كبـري للسـكان النازحيـن مـن الريـف. ويرجـع ذلـك إلـي اتسـام النظـام الحضـري فـي السـودان بالخلـل وعـدم التـوازن إذ يوجـد شـبه غيـاب للمـدن متوسـطة الحجـم والتـي يمكـن أن تكـون حائـط صـد يدفـع النازحيـن بعيـداً عـن مدينـة الخرطـوم الكبـرى وحاجـزاً بينهـا وبيـن ظهيرهـا (عبـد العـال، 1994م، ص: 7).

أدت سـنوات الجفـاف والحـروب الأهليـة والإهمـال التنمـوي الـذي واجهتـه معظـم أنحـاء السـودان إلـي تزايـد مسـتمر لموجـات النازحيـن الجـدد إلـي المـدن الكبـرى، وهكـذا ومنـذ عـام 1970م ازداد تعـداد سـكان الخرطـوم الكبـرى خمسـة

أضعـاف. وكان مـن الطبيعـي أن تـؤدي هـذه الزيـادات السـكانية بدورهـا إلـى زيـادة فـي المسـاحات التـي تغطيهـا المنـازل التـي اسـتقر بهـا هـؤلاء السـكان وعلـى مضاعفة الكتلـة العمرانيـة للمدينـة.

2. مشكلة الدراسة

شـهدت مدينـة الخرطـوم أثنـاء تطورهـا التاريخـي العديـد مـن التغيـرات فـي تركيبهـا التنظيمـي والتخطيطـي، اقتضتهـا موجـات النزوح إليهـا مـن مناطق السـودان المختلفـة، الأمـر الـذي أدي إلـى إشـكاليات تخطيطيـة انعكسـت علـى المظهـر العـام للمدينـة والتركيـب الوظيفـي لأجزائهـا المختلفـة، حيـث كانـت معظـم هـذه الامتـدادات التخطيطيـة علـى أسـس غيـر علميـة، وحتـى مـا تـم مـن عمـل تخطيطـي علمـي كان الغـرض منـه تقنيـن هـذه الامتـدادات وضمهـا إلـى النسـيج الحضـري.

3. أهداف الدراسة

هدفت هذه الدراسة إلى:
1. التعريـف بالخصائـص الطبيعيـة والبشـرية لمدينـة الخرطـوم الكبـرى، ودراسـة أثرهـا علـى النمـو الحضـري للمدينـة.
2. الوقـوف علـى التطـور التاريخـي للنمـو الحضـري لمدينة الخرطـوم الكبـرى.
3. وضـع تصـور مسـتقبلي للنمـو الحضـري لمدينـة الخرطـوم الكبـرى مـن خـلال تطبيـق نمـوذج SLEUTH الرقمـي.

4. منهج وأساليب الدراسة

اعتمـدت الدراسـة علـى عـدد مـن المناهـج والأسـاليب العلميـة لتحقيـق أهدافهـا، تتمثـل فـي المنهـج الوصفـي مـن خـلال دراسـة الخصائـص الطبيعيـة والبشـرية لمنطقـة الدراسـة، والمنهـج الاسـتقرائي مـن خـلال الاعتمـاد علـى تحليـل المخططـات التنظيميـة التـي طبقـت مـن قبـل ووضـع تصـور مسـتقبلي للنمـو الحضـري علـى ضوئهـا.

اسـتخدمت الدراسـة أسـلوب التحليـل المكانـي وأدواتـه مـن خـلال التطبيـق العملـي لـه مـن خـلال برامـج نظـم المعلومـات الجغرافيـة ودراسـة المتغيـرات المختلفـة تبعـاً للبعـد المكانـي للظاهـرة.

5. مصطلحات الدراسة

5.1 النمو الحضري

يعـرف النمـو الحضـري بأنــه الانتشــار والامتـداد خــارج الحـدود الموضوعـة للمدينـة، أي توسـع الهيكـل الحضـري للمدينـة وانتشـاره دون التقيـد بحـدود المناطـق التـي حدثـت فيهـا تلـك العمليـة. كمـا يعـرف كذلـك بأنــه ميـل السـكان للاستقرار فـي المـدن مـن جهـة وتوسـع حجـوم تلـك المـدن مـن جهـة أخـرى ولاسـيما المـدن الكبيـرة، وقـد تكـون هـذه العمليـة قـد تمـت بشـكل عشـوائي غيـر منظـم أو بشـكل علمـي ومخطـط (حسـين،1977م، ص: 27).

5.2 النمذجة

النمـوذج هـو تمثيـل بسـيط للظاهـرة أو النظـام يوضـح المراحـل المختلفـة لتطـور الظاهـرة وعلاقتهـا بالمتغيـرات المكانيـة وغيـر المكانيـة التـي تؤثـر فيهـا وتتأثـر بهـا وإعـادة تصنيـف تلـك العلاقـات ونتائجهـا.

5.3 التحليل المكاني

يعـرف التحليـل المكانـي (Spatial Analysis) بأنـه أسـلوب لقيـاس العلاقـات المكانيـة بيـن الظاهـرات اعتمـاداً علـى قياسـات الموقـع والشـكل والأحجـام والمسـاحات والاتجاهـات والمجـاورة والمطابقـة والارتفـاع والانخفـاض والتصنيـف والتجميـع والترتيـب بغـرض تفسـير العلاقـات المكانيـة والاسـتفادة منهـا وفهـم أسـباب وجـود وتوزيـع الظاهـرات علـى سـطح الأرض والتنبـؤ بسـلوك تلـك الظاهـرات فـي المسـتقبل (شـرف، 2011م، ص:51).

5.4 الخرطوم الكبرى

يجـب التمييـز بيـن مفهـوم مدينـة الخرطـوم الكبـرى ومفهـوم الخرطـوم الولايـة، حيـث يقصـد بالخرطـوم الكبـرى التجمـع الميتروبوليتـي المتكـوّن مـن المـدن الثـلاث (الخرطـوم، أم درمـان، الخرطـوم بحـرى) التـي تنتشـر فيهـا المصالـح والدواويـن الحكوميـة وترتبـط مـع بعضهـا البعـض جغرافيـاً وإداريـاً واجتماعيـاً، أمـا ولايـة الخرطـوم فهـذه تشـمل المـدن الثـلاث وضواحيهـا وبعـض المناطـق المحيطـة بهـا وهـي إحـدى ولايـات السـودان.

6. الدراسات السابقة

تعتبـر الدراسـات التطبيقيـة لنظـم المعلومـات الجغرافيـة مـن الدراسـات الحديثـة خصوصـاً فـي المنطقـة العربيـة، وتتعـدد زوايـا اسـتخدام نظـم المعلومـات الجغرافيـة فـي التخطيـط الحضـري للمـدن فهنالـك دراسـات تركـز علـى عمليـة بنـاء النمـاذج المسـتقبلية للمدينـة ومـن هـذه الدراسـات دراسـة Martin وآخـرون (Martin, Couclelis, & Clarke, 2004)، والتـي تناولـت اسـتخدامات المقاييـس المكانيـة فـي دراسـة تغيـر اسـتخدام الأرض فـي البيئـة الحضريـة، وعملـت الدراسـة علـى خلـق إطـار يجمـع بيـن الاستشـعار عـن بعـد والمقاييـس المكانيـة التـي تهـدف إلـى تحسـين وتحليـل ونمذجـة النمـو الحضـري والتغيـر فـي اسـتخدام الأراضـي. وقـد قـدم الباحثـون نموذجـاً مقترحـاً يـؤدي وضـع تصـورات بديلـة للبنيـة المكانيـة الحضريـة فـي سـانتا باربـرا بولايـة كاليفورنيا. كذلـك مـن الدراسـات دراسـة (الشـمراني، 2003م) وقـد هدفـت الدراسـة إلـى تحليـل النمـو العمرانـي فـي محافظـة الدرعيـة باسـتخدام نظـم المعلومـات الجغرافيـة اعتمـادًا علـى أحـد أسـاليب التحليـل المكانـي المتمثـل فـي اشـتقاق الخرائـط والنمذجـة الكارتوجرافيـة لتحديـد أهـم المتغيـرات التـي تتحكـم فـي النمـو العمرانـي فـي المحافظـة، إضافـة إلـى حسـاب نسـبة النمـو العمرانـي لبنـاء تصـور مسـتقبلي حـول التوسـع العمرانـي بهـا. ومـن الدراسـات دراسـة (Azez, 2004) عملـت هـذه الدراسـة علـى مراقبـة وتوقـع النمـو الحضـري فـي الإسـكندرية مـن خـلال نظـام معلومـات جغرافـي مرتكـز علـى بيانـات الصـور الفضائيـة. هدفـت الدراسـة إلـى تحقيـق عـدة أهـداف فرعيـة تمثلـت فـي تحديـد الخصائـص والسـمات الديموغرافيـة للنمـو الحضـري فـي الإسـكندرية مـن خـلال بيانـات التعـدادات السـكانية ووسـائل القيـاس والتحليـل الديموغرافيـة، تتبعـت الدراسـة النمـو الحضـري للإسـكندرية مـن بدايـة نشـأتها وحتـى نهايـة القـرن العشـرين، وإنتـاج خرائـط توضـح امتـدادات وتوجهـات النمـو الحضـري فـي الإسـكندرية باسـتخدام مناهـج وتقنيـات اسـتكشاف التغيـر الزمنيـة والمكانيـة المتعـددة، والوقـوف علـى تبعـات هـذا التمـدد الحضـري.

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7. خصائـص منطقـة الدراسـة واثرهـا علـى النمـو الحضـري

7.1 الموقع الجغرافي

تقـع منطقـة الدراسـة بيـن خطـي طـول °31.5 - °34 شـرقاً ودائرتـي عـرض °16-°15 شـمالاً تقريبـاً ومسـاحتها حوالـي 165.28 كـم مربـع. يحدهـا مـن الجهـة الشـمالية والجهـة الشـرقية ولايـة نهـر النيل ومـن الجهـة الشـمالية الغربيـة الولايـة الشـمالية، ومـن الجهـة الشـرقية والجنوبيـة الشـرقية ولايـات كسـلا القضـارف والجزيرة (حكومـة ولايـة الخرطوم، 2016م)، والشـكل (1) يوضـح موقـع ولايـة الخرطـوم فـي خريطـة السـودان والولايـات المحيطـة بهـا.

7.2 الخصائص الديموغرافية لمدينة الخرطوم الكبرى

تعتبـر ولايـة الخرطـوم الأولـى فـي الترتيـب مـن حيـث حجـم السـكان بالنسـبة لولايـات السـودان وفقـاً لتعـداد السـكان والمسـاكن الخامـس الـذي أجـري فـي العـام 2008م، حيـث بلـغ حجـم سـكانها الكلـي 5181186 نسـمة، الذكـور منهـم 2725185 والإنـاث 2456002 مقارنـة بحجـم 3.4 مليـون فـي العـام 1993م، الذكـور منهـم 1882000 والإنـاث 1631000 بينمـا الحجـم 1.8 مليـون فـي العـام 1983م، الذكـور منهـم حوالـي 976000 نسـمة والإنـاث 826000 نسـمة.

نسـبة النـوع وفقـاً لتعـداد 2008م بلـغ 111 ذكـر لـكل 111 أنثـى مقارنـة بـ 115 وفقـاً لتعـداد 1993م و 118 وفقـاً لتعـداد 1983م. وبلـغ معـدل النمـو 2.7% بيـن تعـداد 1993م وتعـداد 2008م، ومعـدل نمـو 6.56% بيـن تعـداد 1983م وتعـداد 1993م. وطبقـاً للتقديـرات المسـتقبلية للسـكان والمبنيـة علـى الجـدول (1) سـيتضاعف حجـم السـكان فـي مدينـة الخرطـوم الكبـرى خـلال أقـل مـن 20 عامـاً ولـذا لابـد مـن الاهتمـام بوضـع الخطـط والبرامـج المناسـبة التـي توفـر الاحتياجـات الأساسـية مـن فرص عمـل وخدمـات تتمثـل فـي الصحـة والتعليـم والميـاه والصـرف الصحـي والكهربـاء والطـرق والاتصـالات لهـذه الزيـادة فـي السـكان مـع تأميـن هـذه الاحتياجـات حاليـاً والتـي تتفاقـم مشـاكلها يومـاً بعـد يـوم.

8. النمـو الحضـري المخطـط لمدينـة الخرطـوم الكبـرى

مـرت مدينـة الخرطـوم الكبـرى خـلال فتراتهـا التاريخيـة بعـدة

تحـولات مـن حيـث التركيـب الحضـري والعمرانـي ومـن حيـث التركيـب الديموغرافـي والاجتماعـي، حيـث يـري كثيـرون أن بدايـة الوجـود الحضـري لمدينـة الخرطـوم كان مـن خـلال حضـارة سـوبا، وقـد تباينـت أشـكال النمـو الحضـري خـلال الفتـرات التاريخيـة المختلفـة فتـارة كانـت تتخـذ النمـط المخطـط للنمـو وفـي معظـم الأحيـان تتخـذ النمـط غيـر مخطـط.
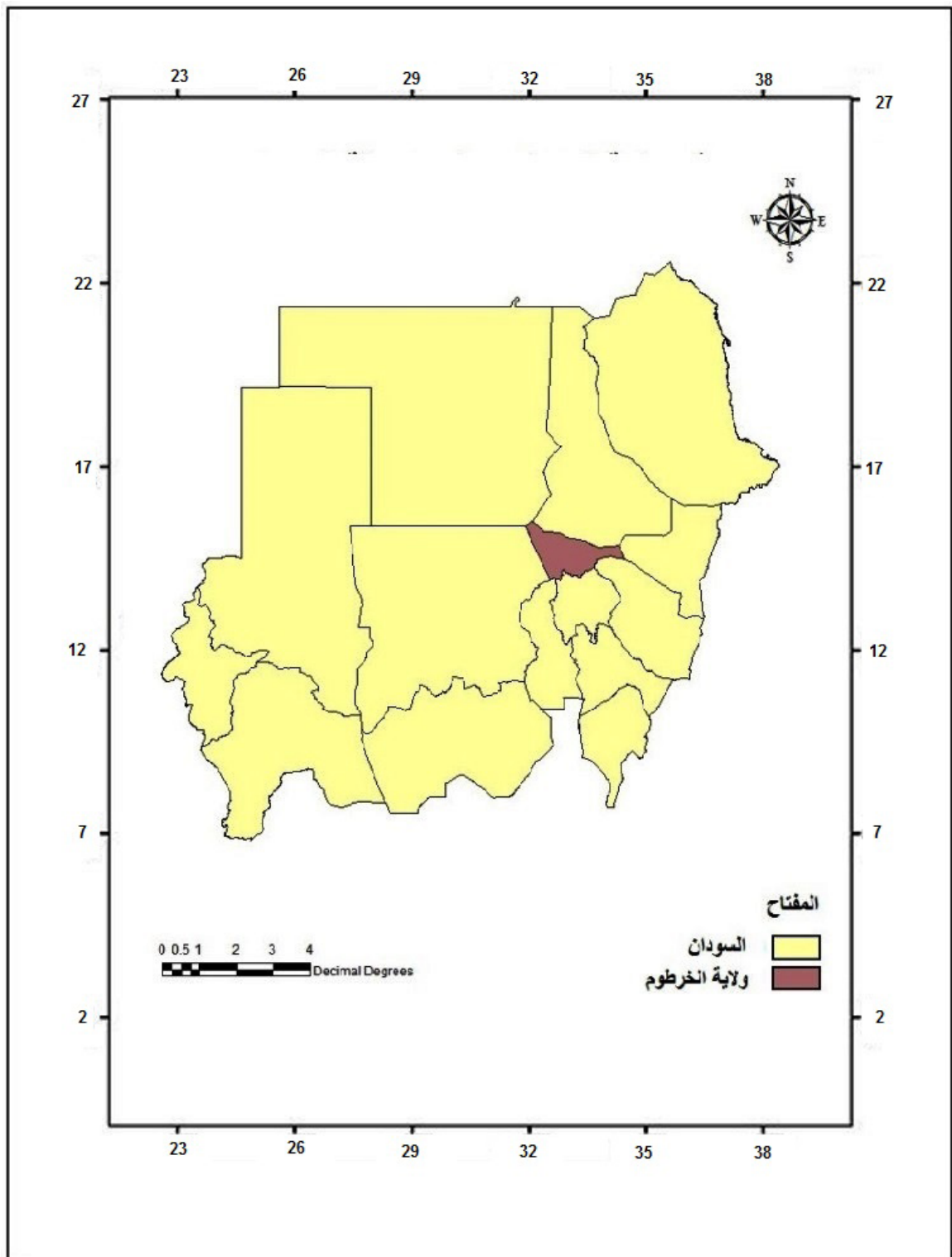
جدول 1: التطور السكاني لولايـة الخرطوم (الجهاز المركزي للإحصاء، 2008م).

معدل النمو (%)	نسبة سكان الولاية لسكان السودان (%)	عدد السكان (نسمة)	السنة
2.13	2.53	260.599	1956م
2.57	5.75	808.000	1973م
2.88	6.52	1.805.567	1983م
2.70	13.34	3.413.700	1993م
2.53	17	5.181.186	2008م

8.1 النمو الحضري مـا قبل الحكم الثنائي

تميـزت السـمات الحضريـة للدولـة ككل فـي فتـرة التركيـة السـابقة بالآتـي:

• تغلـب سمات الحياة الريفية والبدوية.
• لم تنشأ مدن في تلك الفترة بالمعنى الحديث.
• اعتمد الأتـراك الخرطوم عاصمة للبـلاد عندهـا ظهـرت بعض المـدن كعواصـم إقليميـة ومراكـز للحكـم والإدارة القبليـة والعبـادة والتجـارة.
• اعتمـد الأتـراك علـى أنقـاض سـوبا فـي بنـاء قصـر الحاكـم، وتـم اسـتجلاب عمـال مهـرة مـن مصـر وبعـض مـواد البنـاء، ثـم تعليـم الأهالـي كيفيـة البنـاء وكيفيـة تحضيـر الطـوب المحـروق والجيـر، وظهـرت أسـاليب البنـاء الحديـث.
• لـم يتبـع ذلـك تطـور فـي تنظيـم وتخطيـط الوحـدات السـكنية وتحديـد الاحتياجـات لمجمـوع الوحـدات السـكنية بطريقـة مدروسـة.
• لم يتعد سكان العاصمة آنذاك 45.000 نسمة.

أمـا فتـرة المهديـة فقـد تمركـز الوجـود الحضـري فـي مدينـة أم درمـان حيـث اختارهـا المهـدي لتصبـح معسـكراً لجيـوش المهديـة، تطـور هـذا المعسـكر لتصبـح أم درمـان عاصمـة

شكل 1: موقع ولاية الخرطوم في خريطة السودان (الجهاز المركزي للإحصاء ، 2016م).

8.3 فترة ما بعد الاستقلال (1956 - 2010م)

شــهدت هـذه الفتــرة الامتـدادات الكبيـرة لمدينـة الخرطوم وتحولهـا إلـى مدينـة واسـعة المسـاحة ومترامية الأطـراف، مـع غلبـة الاستخدام السكني علـى بقيـة الاستخدامات لمقابلـة الطلــب المتزايـد علـى الأراضـي السـكنية كنتــاج طبيعـي لزيـادة عـدد السـكان. ومـن أهـم الخطـط التـي وضعـت فـي هـذه الفتــرة.
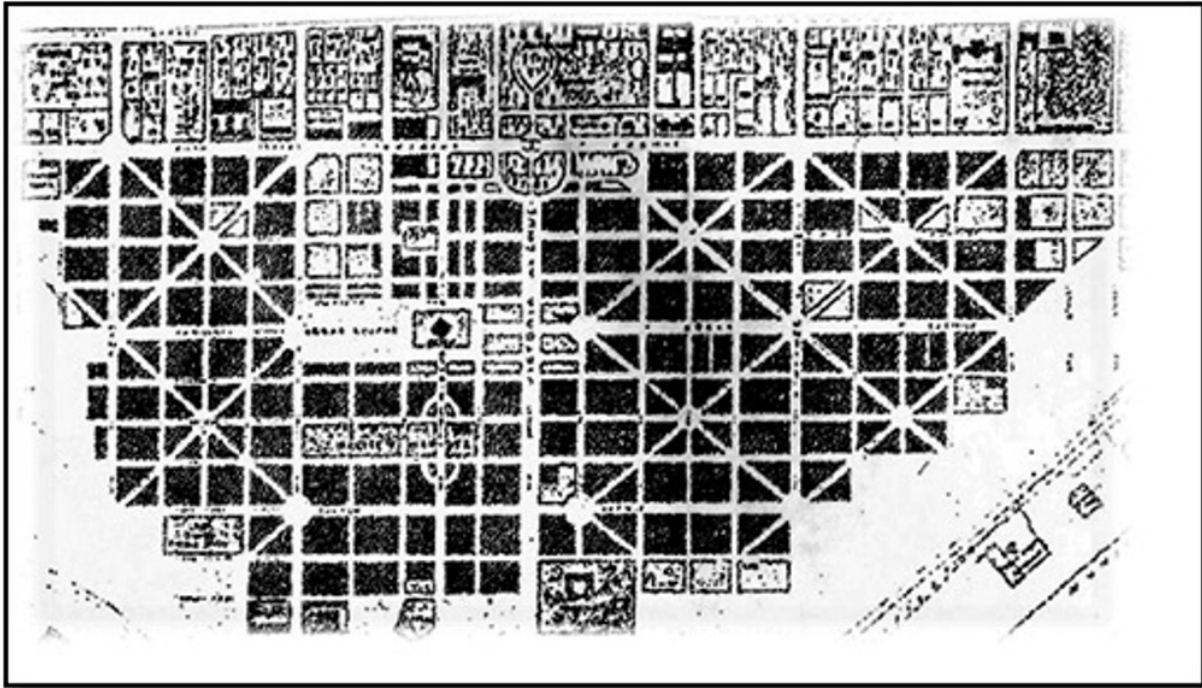
8.3.1 المرحلة الأولى

شــملت هـذه المرحلـة عـدداً مـن الخطـط العمرانيـة ذات الخصائـص المختلفـة، واجهـت هـذه الخطـط عـدداً مـن الإشكاليات التـي لـم تسـمح بتطبيقهـا بشـكل سـليم، وهـذه الخطـط هـي:

- خطـة مجموعة دوكسيادس 1959م.
- خطـة شـركة مفت الإيطاليـة لتطويـر الخرطـوم الكبـرى 1974م.
- لخريطـة الموجهة للتنمية العمرانية لولاية الخرطوم 1990 - 2000م.

الدولـة وبذلـك أهملـت الخرطــوم وتهدمـت مبانيهـا وهجرت. وتدريجيـاً أصبحـت مبانـي أم درمـان تبنـى بمـواد ثابتـة، وتحولـت إلـى مسـتوطنة مسـتقرة وعاصمـة لدولـة المهديـة. وشـكل المسـجد المركـزي مركـزاً للعاصمـة الجديـدة (مـادبـو وأبـو القاسـم، 2012م، ص:3).

8.2 فترة الحكم الثنائي (1898 - 1955م)

ظهـرت أول أشـكال النمـو العمرانـي الموجـه بالمعنـى العلمـي الحديـث فـي فتـرة الاحتـلال الثنائـي الانجليـزي المصـري، حيـث تـم اعتمـاد عـدد مـن الخطـط العمرانيـة. ومـن أهـم ملامـح هـذه الفتـرة اعتمـاد النظـام الشـبكي مـع إدخـال الشـوارع الوتريـة عنـد التقاطعـات المتعامـدة (نسـق تخطيـط الاستحكامـات الأمنيـة لتوطيـد أركان المسـتعمر)، كمـا تـم تقسـيم المدينـة إلـى أربعـة قطاعـات: القطـاع الحكومـي، القطـاع التجـاري، قطـاع الصناعـات الحرفيـة والقطـاع السـكني، ومـن أهـم المخططـات فـي تلـك الفتـرة (مخطـط كتشـنر، مخطـط مـك ماكلينـز، مخطـط عبـد المجيـد صالـح، مخطـل ل. كولمـان)، والشـكلان (2 و 3) يبـرزان أهـم هـذه المخططـات.

شكل 2: مخطـط كتشـنر لمدينـة الخرطـوم عـام 1902م (التقاطعـات علـى شـكل العلـم البريطانـي UN - Ha)، (وزارة التخطيـط والتنميـة العمرانيـة ولايـة الخرطوم، 2010م؛ UN-Habitat, 2008).
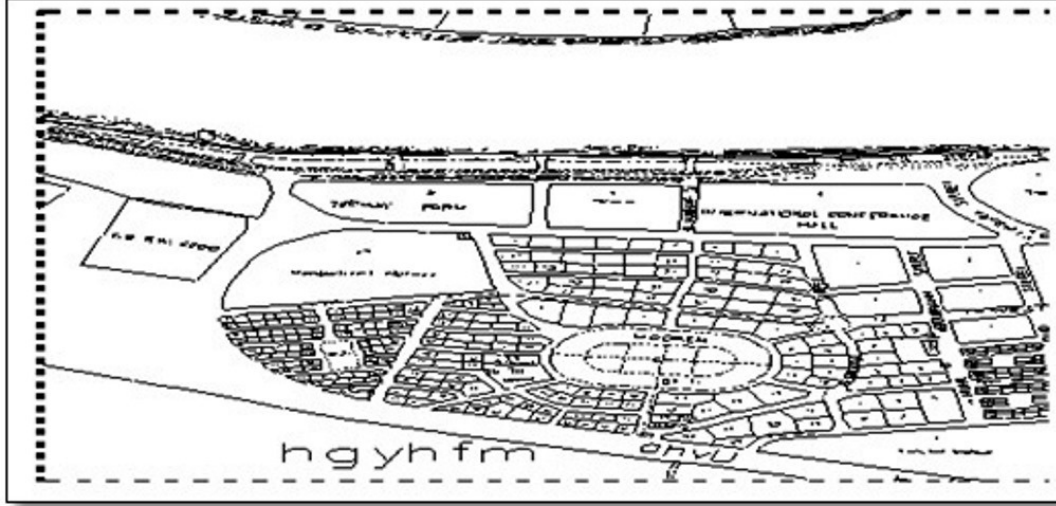
شكل 3: مخطط عبد المجيد صالح لمدينة الخرطوم (وزارة التخطيط والتنمية العمرانية ولاية الخرطوم، 2010م).

والشـكل (4) يوضـح النمـو الحضـري المخطـط لمدينـة الخرطـوم فـي الفتـرة مـن (1956– 2010م).
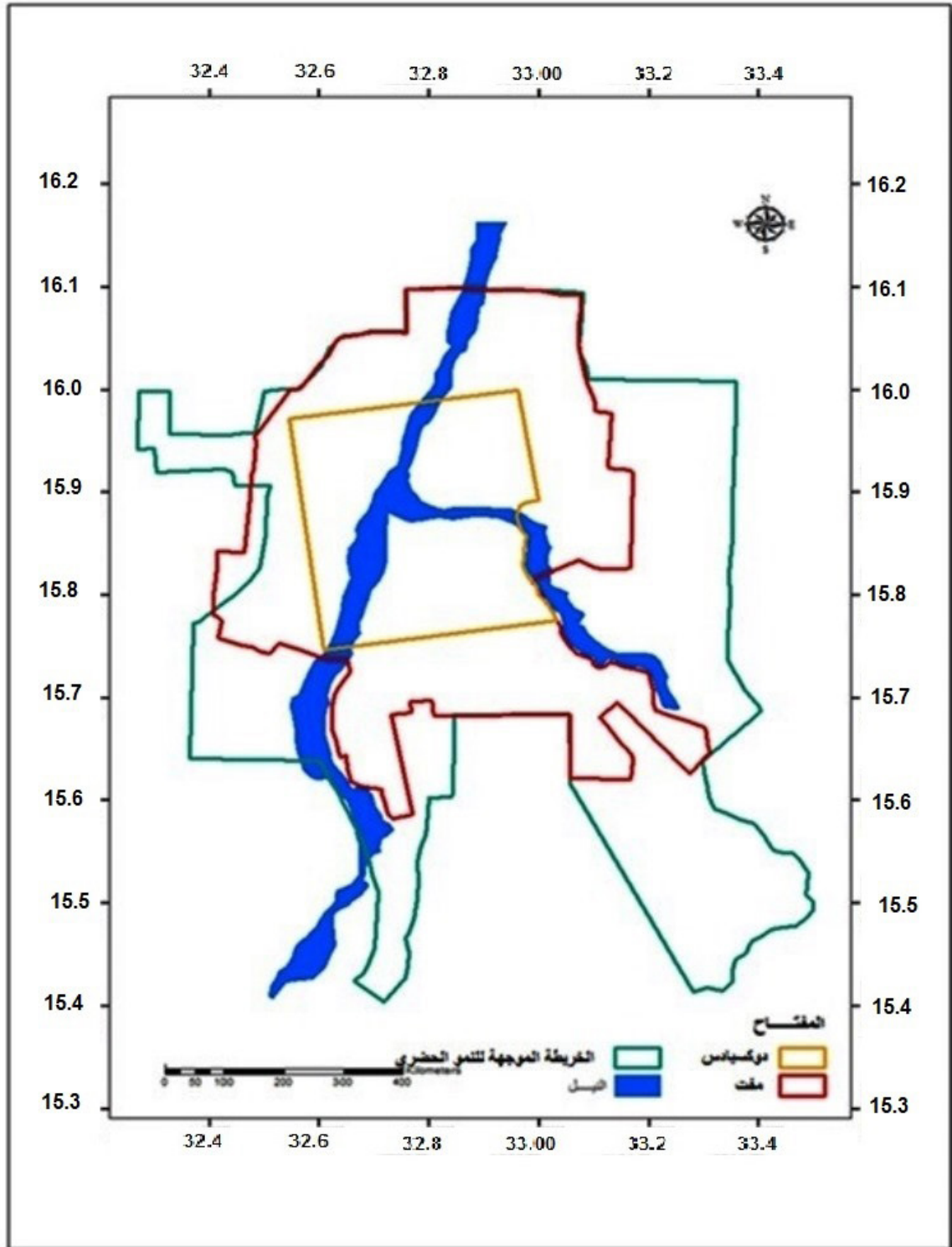
8.3.2 المرحلة الثانية

8.3.2.1 الخطـة الهيكليـة لتنميـة وتطويــر الخرطـوم الكبــرى 2010 - 2035م

دمـج المخطـط الهيكلـي لولايـة الخرطـوم مـا بيـن العمليـات والإجراءات ومقـومات التحضـر للعاصمـة الخرطـوم، والحاجـة إلـى التخفيـف مـن النقص المتراكـم في وضـع الأسـس والمتطلبات المسـبقة للنمـو المسـتقبلي. صممـت الخريطـة الهيكليـة للخرطـوم وفـق منظـور زمنـي مبنـي علـى توقـع افتراضـي لثلاثـة أسـاليب عمليـة هامـة تـؤدي إلـى وضـع حضـري وتنميـة إقليميـة متوازنـة ومسـتدامة وتنافسـية وذلـك بتعريـف: قضايـا الوضـع الراهـن والقضايـا المتراكمـة للتنميـة الحضريـة والإقليميـة، مأسسـة إطـار

للتنميـة الحضريـة والإقليميـة المسـتدامة ووضـع وتطبيـق نظـام فعـال لـلإدارة والإجـراءات الماليـة للأغـراض التنفيذيـة. وقـد تـم وضـع عـدة مسـتويات تخطيطيـة للمخطـط الهيكلـي مـن أهمهـا هيـكل التنميـة الحضريـة والـذي تـم تأسيسـه علـى إيقـاف التمـدد الأفقـي للعاصمـة وإنشـاء الطريـق الدائـري الخارجـي كحاجـز طبيعـي لرسـم حـدود المنطقـة الحضريـة، وإن اسـتيعاب أي نمـو حضـري مسـتقبلي سـيكون مـن خـلال آليـة التكثيـف فـي سـياق التجديـد الحضـري، أمـا مـن الناحيـة الإسـتراتيجية فـإن التطـور الحضـري للخرطـوم سـيكون مبنيـاً علـى إنشـاء تسـعة مـدن جديـدة لاسـتيعاب أكثـر مـن سـتة مليـون نسـمة خـلال الخمسـة وعشـرين عامـا القادمـة (المخطـط الهيكلـي العمرانـي الخامـس، 2010م، ص: 44). والشـكل (5) يوضـح الخريطـة الهيكليـة وفـق المخطـط الهيكلـي المعتمـد لولايـة الخرطـوم، كمـا يوضـح الجـدول (2) مسـار الخطـط الهيكليـة السـابقة لولايـة الخرطـوم ونسـبة الإنجـاز فيهـا مـع مسـار المخطـط الهيكلـي المعتمـد حتـى العـام 2023م.

جدول 2: مسار الخطط الهيكلية الأربعة السابقة لولاية الخرطوم ونسبة الإنجاز 2007-1912م (وزارة البيئة والغابات والتنمية العمرانية ولاية الخرطوم وجامعة الزعيم الأزهري، 2010م).

نسبة الانجاز	الكثافة المستهدفة	المساحة الحضرية الإجمالية (كلم²)	عدد السكان المستهدف (نسمة)	الخطة
90%	87	11.5	100.000	مخطط ماكلينز 1912م
40%	44	182	793.000	مخطط دوكسيادوس 6019-1980م
20%	23	1103	2.500.000	مخطط مفت الإقليمي 7519-1995م
15%	37	1441	5.300.000	مخطط دوكسيادس وعبد المنعم 1990-2000م
؟	50	1650	7.000.000	المخطط الهيكلي العمراني مفت وستنكس2007-2023م

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شكل 4: النمو الحضري المخطط لمدينة الخرطوم الكبرى.
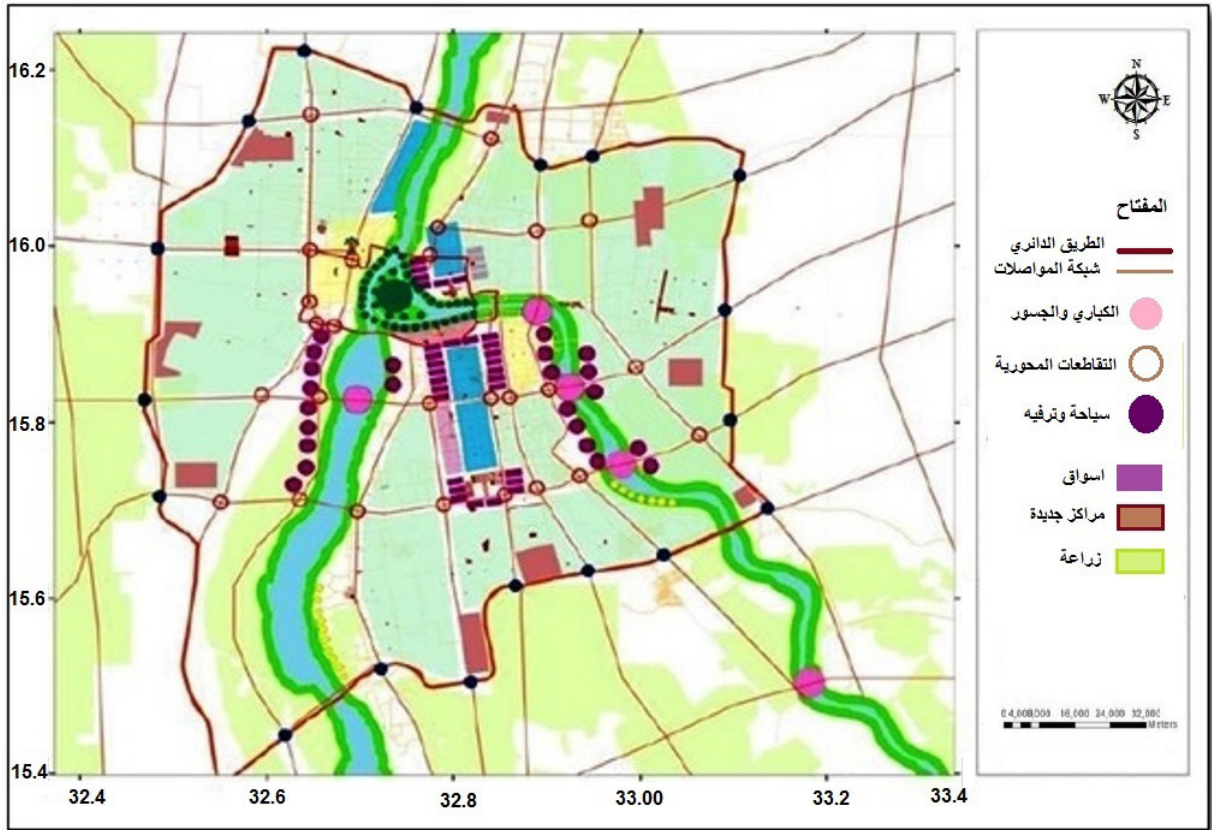
9. نمذجة النمو الحضري لمدينة الخرطوم الكبرى

نتيجـة للنمـو الحضـري السـريع وتغيـر اسـتخدام الأرض فـي المـدن اتجـه العلمـاء للبحـث عـن طرائـق تمكنهـم مـن توقـع النمـو والتغيـرات المسـتقبلية ممـا يمكنهـم مـن رسـم سـيناريو لمـا سـيحدث فـي المسـتقبل، ومـن ثـم العمـل علـى تلافـي الآثـار السلبية المتوقعـة، وفـي سـبيل ذلـك تـم تطويـر عـدد مـن النمـاذج الرقميـة اطلـع الباحـث علـى عـدد منهـا. وكـل هـذه المجهـودات تهـدف إلـى بنـاء شـكل نموذجـي للمدينـة، إلا أن هـذه النمـاذج علـى الرغـم مـن تركيبها العلمـي السـليم لا يمكـن الاعتمـاد عليهـا فـي هـذه الدراسـة وذلـك لثلاثـة أسـباب، الأول هـو: أن التنميـة الحضـرية عـادة لا تتبـع أي خطـة بسـيطة. وأن نمـاذج النمـو الحضـري عـادة مـا تخضـع إلـى عمليـات توسـع مـن الخـارج ممـا يـؤدي إلـى خلـق واقـع أبعـد مـا يكـون عـن الخطـة الأساسـية وأكـثر تنوعـا وتعقيـداً. والسـبب الثـاني هـو: أن وضعـت هـذه

النمـاذج لشـرح حضـرية النمـو فـي الولايـات المتحـدة وأوروبـا بحيـث لا يكـون لديهـم أي نيـة لتبريـر النمـو الحضـري خـارج هـذه المناطـق، وعـلاوة علـى ذلـك فـإن العوامـل التـي تدفـع المناطـق الحضـرية للنمـو فـي هـذه المناطـق هـي مختلفـة تمامـاً عـن نظيراتهـا فـي البلـدان الناميـة، والسـبب الثالـث أن كـل مدينـة لهـا طابعهـا الخـاص وفقـاً لعوامـل معقـدة كثيـرة عوامـل منهـا الثقافـة، والوضـع الاقتصـادي... الـخ.

9.1 النموذج المستخدم لقياس النمو الحضري
9.1.1 مصادر معلومات النموذج المستخدم

اعتمـدت الدراسـة علـى نسـخة معدلـة مـن نمـوذج SLEUTH للنمـو الحضـري أو نمـوذج كلارك للنمـو الحضـري وهـو مـن تطويـر فريـق عمـل برئاسـة جغرافـي أمريكـي يدعـي كيـث كلارك Keith Clarke (Clarke, 1997) وهـذا النمـوذج

شكل 5: المخطط الهيكلي لولاية الخرطوم 2010م، (وزارة التخطيط والتنمية العمرانية ولاية الخرطوم، 2010م).

المعدل قد استخدمه الباحث لطفي كمال عزيز (Azez, 2004) في دراسته عن النمو الحضري لمدينة الإسكندرية، وتم فيه مراعاة الخصائص الطبيعية البشرية للمدن العربية. اسم النموذج SLEUTH مشتق من المدخلات التي يستخدمها، فحرف S يرمز للانحدار (Slope) وحرف L يرمز لاستخدام الأرض (Land Use)، وحرف E يرمز للمناطق المستبعدة من النمو المستقبلي (Exclusion)، وحرف U يرمز للامتداد الحضري (Urban Extent)، وحرف T يرمز لشبكة المواصلات (Transportation)، وحرف H يرمز للظل التضاريسي (Hillshade) الذي يستخدم كخلفية لمخرجات النموذج، ويعمل النموذج من خلال تحديد قاعدة تخطيطية للنمو يتم تطبيقها مكانياً باستخدام خرائط المدخلات السابقة ومنها يتم التعرف على كيفية حدوث النمو الماضي والحاضر، ويتم ذلك من خلال مطابقات مكانية معتمدة على طبقات(raster) يمكن من خلالها تطبيق النموذج.

وبالإضافة إلى الطبقات السابقة وتضمينها في النموذج فإنه احتوى أيضاً عملية رياضية أخرى خاصة بالعلاقة بين التوسع الحضري والنمو السكاني في مدينة الخرطوم، حيث توصلت الدراسة من خلال دراسة النمو السكاني للمدينة من خلال التعدادات السكانية التي تمت بها (1956م، 1983م، 1993م، 2008م) ودراسة التوسع الحضري للمدينة لنفس الفترات إلى أن كل زيادة بمعدل 1% من النمو السكاني يؤدي إلى 1.9% في التوسع الحضري وبالتالي يفترض النموذج أن معدلات التطور الحضري سوف تكون بنفس المعدلات الحالية تجاه العلاقة مع زيادة السكان.

9.1.2 إعادة تصنيف الطبقات بناء على القيمة الرقمية للبكسل

إن التحويل من vector إلى raster لأي نقطة يعطي قيمة لأي عقدة (pixel)، وهذه القيمة تتوقف على اختيار المستخدم. تمت عملية التحويل باستخدام قيمة 75 متر لكل بكسل،
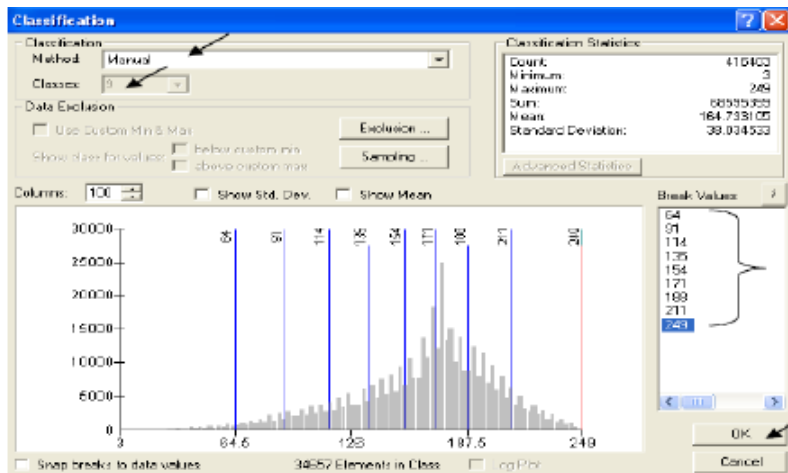
وبالتالي أصبحت النقطة تقابل واحد بكسل أبعاده 75 متراً من كل جانب. وأصبح الخط يقابل سلسلة من البكسلات والمساحة تحتوي على عدد من البكسلات تختلف باختلاف حجم المساحة زيادة أو نقصاناً. إلا انه بسبب هذه العملية فقدت بعض المعلومات (خاصة في ما يختص بشبكة الطرق). لذلك تم استخدام إبعاد مختلفة للبكسلات للتقليل من حجم الفاقد من المعلومات. والشكل (6) يوضح عملية إعادة تصنيف الطبقات المكونة للنموذج بناءً على القيمة الرقمية للبكسل.

وبناءً على ما سبق تم تحديد عدد الدرجات المطلوبة لكل طبقة من الطبقات المكونة للنموذج، بعد ذلك يتم تركيب المعلومات المكانية الطوبولوجية تحت شكل شبكي أو grid، والشكل (7) يوضح ذلك.

ومن ثم عمل الباحث على تحويل جميع الطبقات المطلوبة

شكل 6: إعادة تصنيف الطبقات بناء على القيمة الرقمية للبكسل.

شكل 7: تركيب المعلومات المكانية بشكل شبكي.

في النمـوذج إلـى صيغـة الـ Raster. بعـد الحصـول علـى الطبقـات المطلوبـة والتـي تتمثـل فـي الانحـدار (Slope) واسـتخدامات الأرض (Land Use)، والمناطـق المسـتبعدة مـن النمـو المسـتقبلي (Exclusion) والتـي تتمثـل فـي نهـر النيـل والمناطـق المخصصـة للنشـاط والغابـي والزراعـي. وللامتـداد الحضـري (Urban Extent). وشـبكة المواصـلات (Transportation) بالإضافة إلـي الظـل التضاريسـي (Hillshade). والأشـكال (8، 9، 10، 11) توضـح ذلـك.
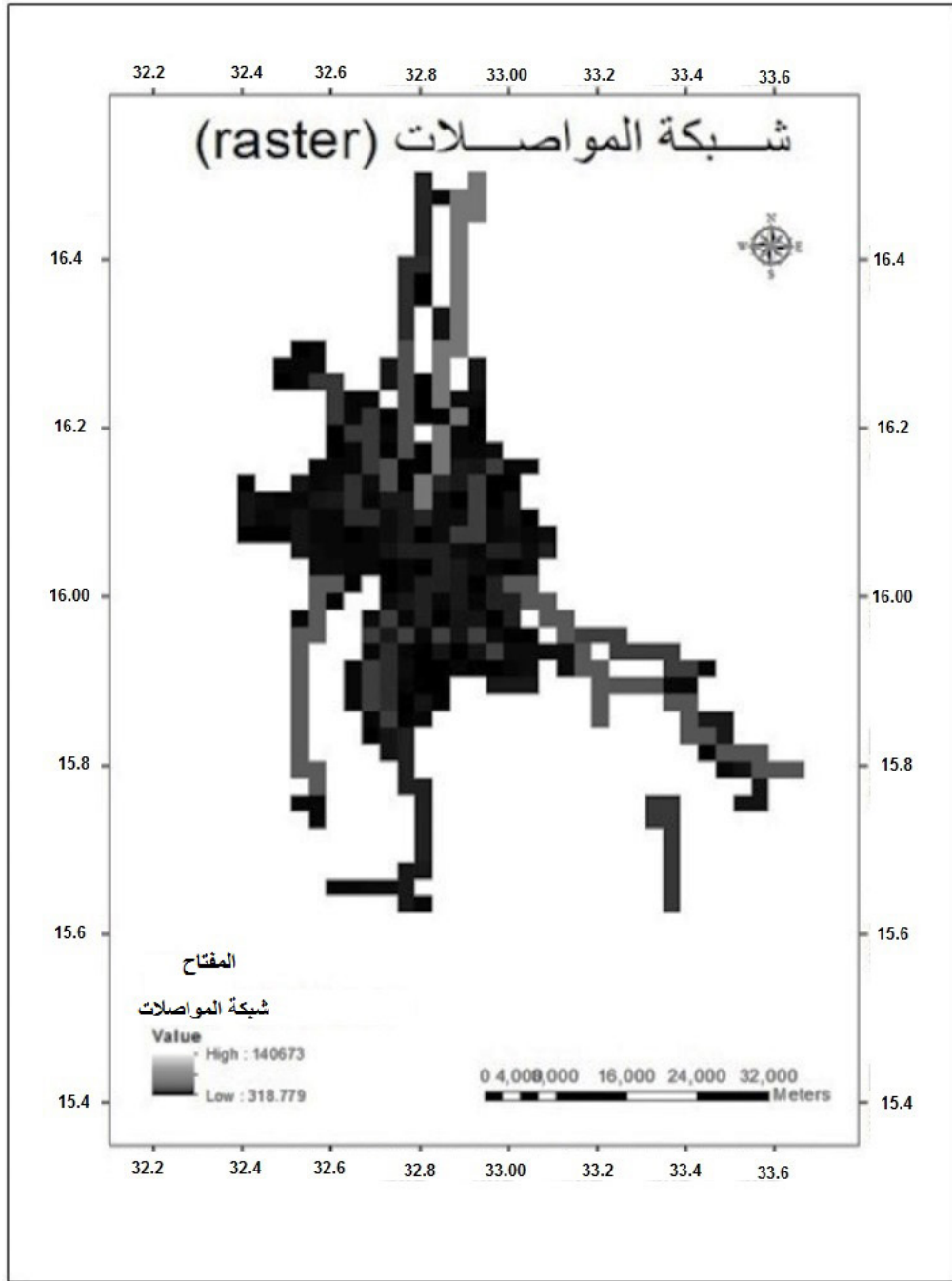
شكل 8: الاشتراطات المكانية حسب نموذج SLEUTH (شبكة المواصلات – Raster).

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المناطق المستبعدة من النمو المستقبلي (raster)

المفتاح

المناطق المستبعدة

Value
High : 221674

Low : 56.9542

07,000,000 28,000 42,000 56,000
Meters
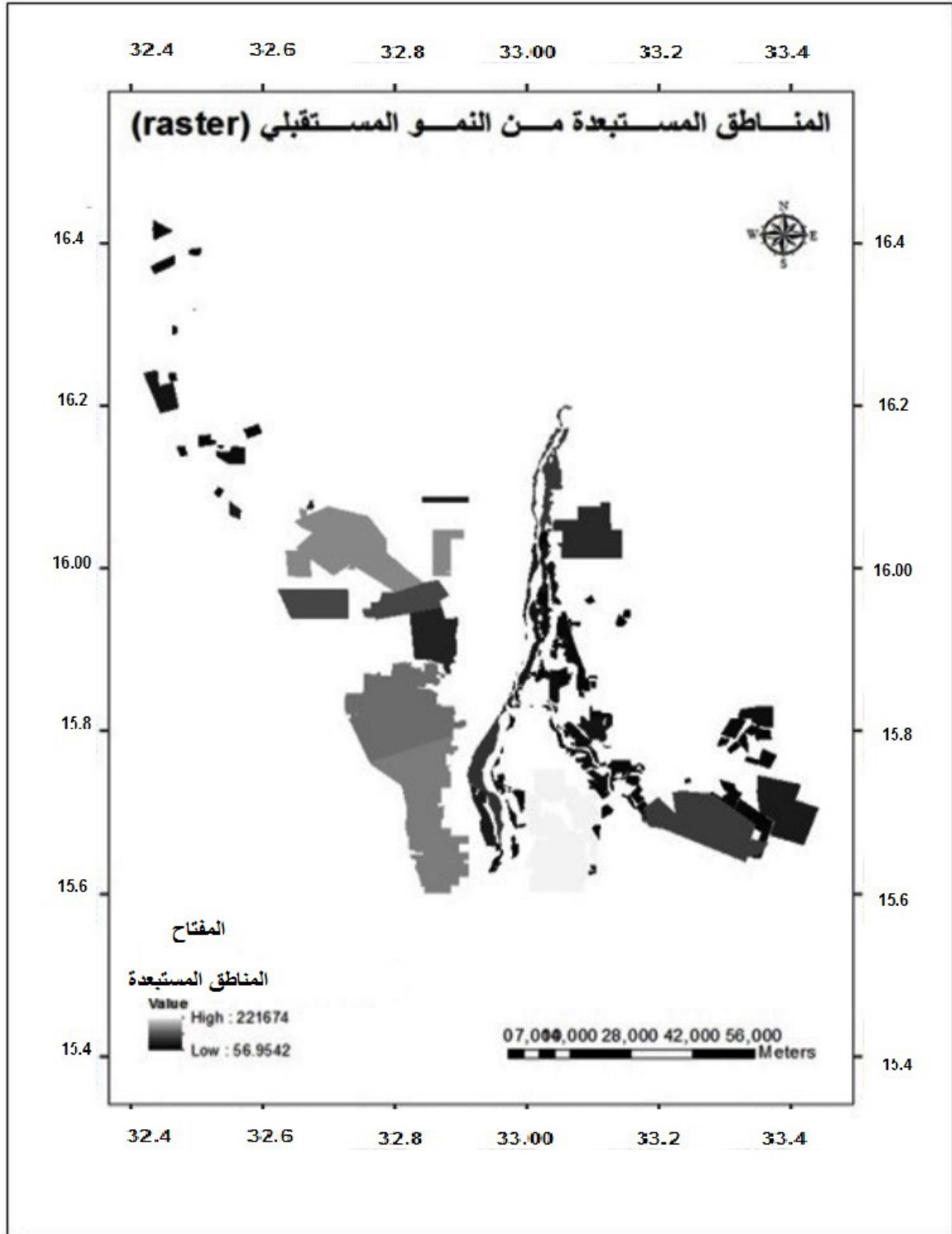
شكل 9: الاشتراطات المكانية حسب نموذج SLEUTH (المناطق المستبعدة - Raster).
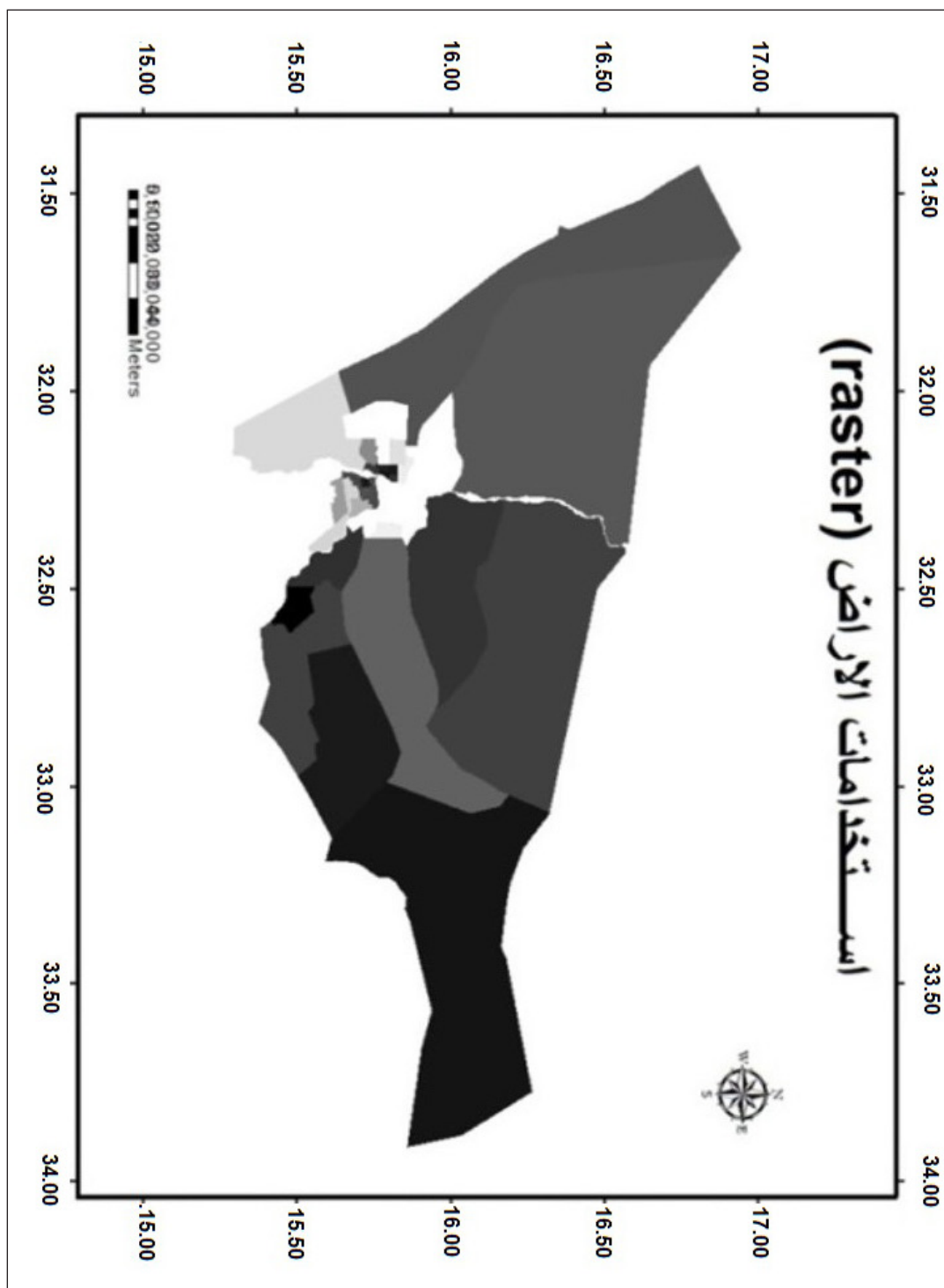
شكل 10: تمثيل الطبقة الشبكية SLEUTH (السليمات الإدراك - Raster).
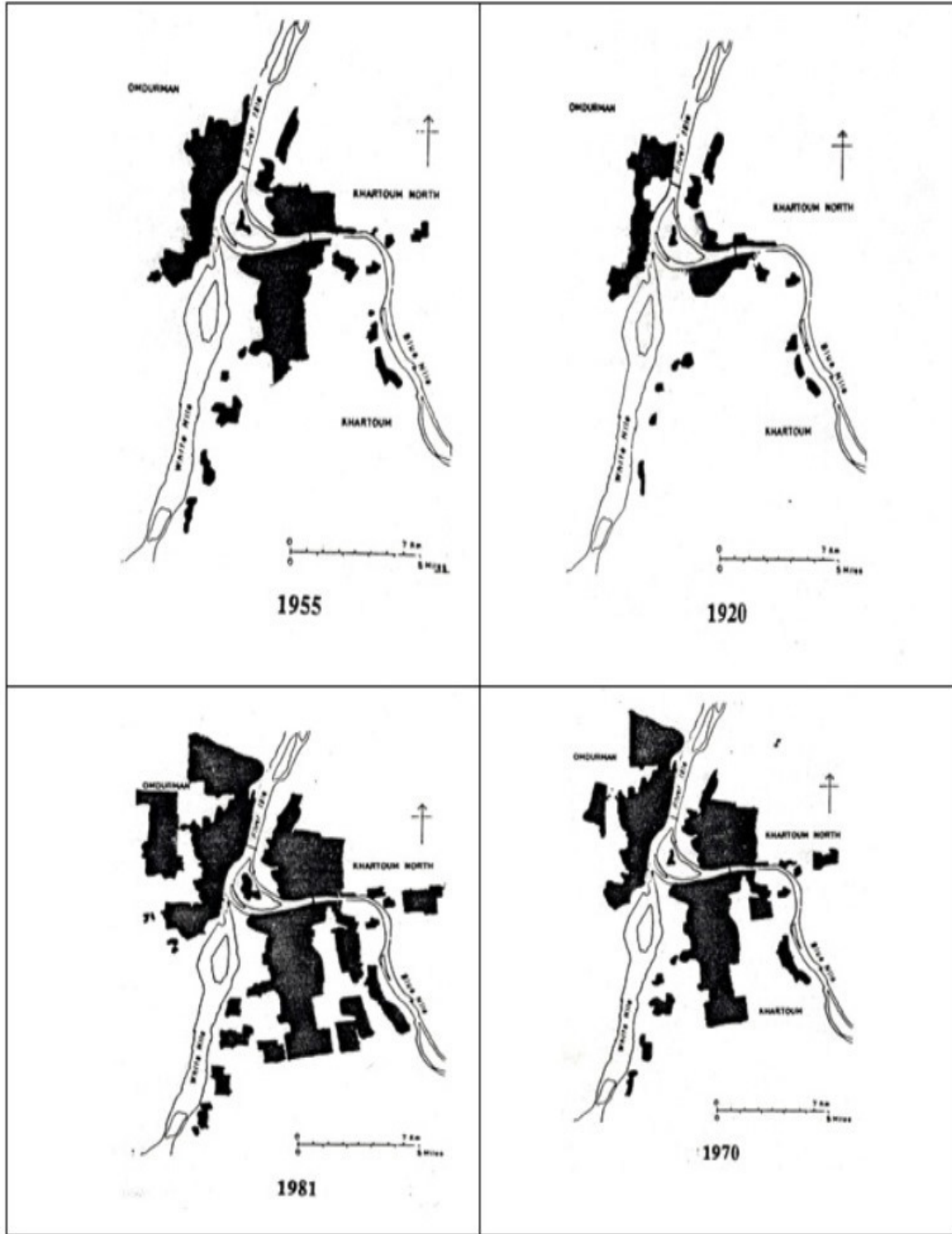
شكل 11: الاشتراطات المكانية حسب نموذج SLEUTH (الامتداد الحضري والظل التضاريسي – Raster)، (وزارة التخطيط والتنمية العمرانية ولاية الخرطوم، 2010م).

2.9 خطوات بناء النموذج

لبنـاء النمـوذج تـم التعامـل مـع المدخـلات التـي تـم التوصـل اليهـا فـي الخطـوات السـابقة والمتمثلـة فـي الطبقـات المختلفـة المكونـة للنمـوذج، بالإضافـة معـدل النمـو الحضـري السـنوي المتحصـل عليـه والبالـغ 1.9%. وتتمثـل الخطـوات التطبيقيـة فـي برنامـج ArcGIS 10 فـي الخطـوات التاليـة:

1. سـحب الطبقـات المكونـة للموديـل مـن جـدول المحتويـات إلـى نافـذة الموديـل.

2. فتـح صنـدوق الأدوات 3D Analyst مـن Arc Toolbox.

3. فتـح Conversion.

4. فتـح From TIN.

5. سـحب الأداة إلـى الموديـل مرتيـن للطبقـة الحاليـة والطبقـة المتوقعـة.والشـكلان (12 و 13) يوضحـان بنـاء النمـوذج للطبقتيـن الحاليـة والمتوقعـة.

ينتـج عـن الخطـوة السـابقة خصائـص الطبقـة الحاليـة للنمـو
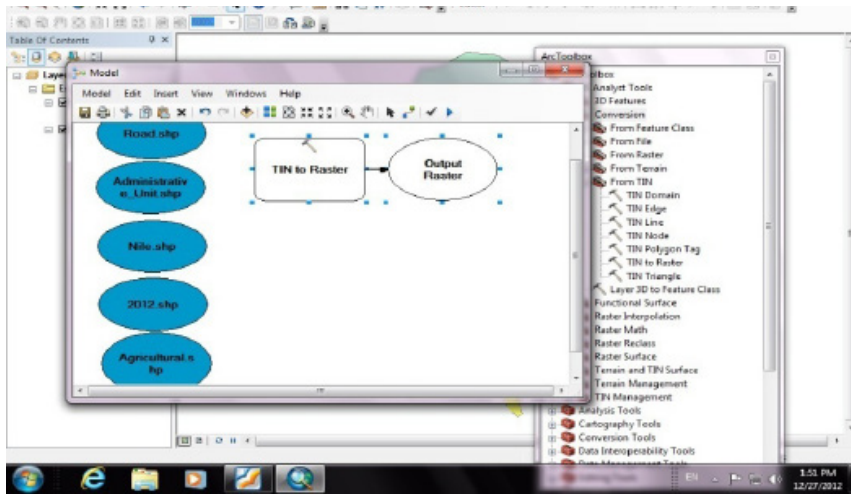
شكل 12: إنشاء النموذج في برنامج Arcgis10 (الطبقة المتوقعة).

شكل 13: إنشاء النموذج في برنامج Arcgis10 (الطبقة المتوقعة).

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الحضـري، وخصائـص الطبقـة المسـتقبلية للنمـو الحضـري. ومـن ثـم يتـم تطبيـق العمليـات الحسـابية الخاصـة بالعلاقـة بيـن التوسـع الحضـري والنمـو السـكاني. وذلـك مـن خـلال الخطـوات التاليـة: يتـم تحويـل الـ 1 - (Output Raster) إلـى tgrid – after (Output Raster) - 2 و tgrid – إلـى before في الموديـل. ومـن ثـم سـحب أداة Single Output

Map Algebra مـن Arc Toolbox إلـى نافذة الموديل كمـا هـو موضـح فـي الشـكل (14).
بعـد الخطـوة السـابقة قـام الباحـث بالتعامـل مـع أداة Surface Volume مـن Arc Toolbox لإدراج الطبقـات الناتجـة مـن أداة Map Algebra وتوصـل هذه الأداة مـع الطبقتيـن كمـا هـو موضـح فـي الشـكل (15).
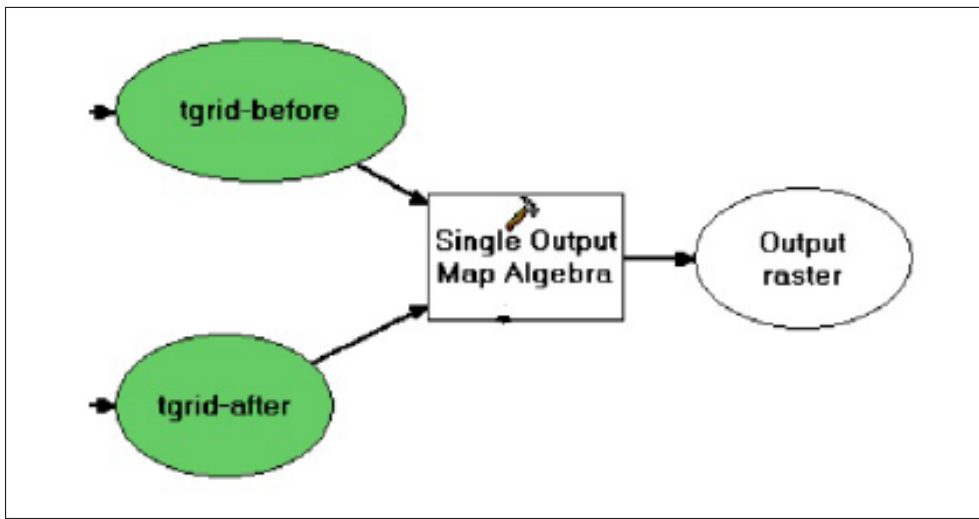
شكل 14: استخدام المعادلات الجبرية لتطبيق العمليات الحسابية الخاصة بالتوسع الحضري.
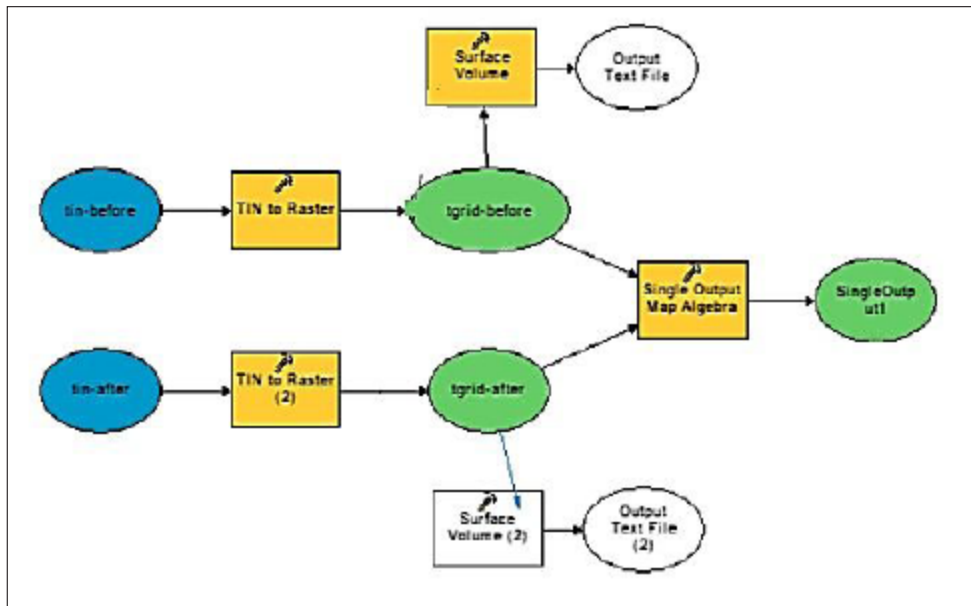
شكل 15: النموذج بشكله النهائي.

9.2.1 ملاحظــات حــول الخريطــة المنتجــة بنــاءاً علــى تطبيــق النمــوذج

من خــلال الخريطــة (شكل 16) يمكن أن نوضـح الملاحظــات التالية:

بعد تطبيق الخطــوات الســابقة يصبـح لدينا نمــوذج للتوسـع الحضري لمدينــة الخرطــوم حتــى عــام 2033م، وذلك مـع افتــراض أن شــروط التمــدد الحضــري ســواء كانـت السكانية أو العمرانيـة لــن تتغيــر خــلال هذه الفترة. والشــكل (16) يوضـح النمـو الحضري المتوقع لمدينــة الخرطــوم حتــى عــام 2033م بتطبيــق نمــوذج SLEUTH.

شكل 16: النمو الحضري في مدينة الخرطوم حتى عام 2033م بتطبيق نموذج SLEUTH.

1. توصلت الدراسة إلى أن كل زيادة بمعدل 1% من النمو السكاني يؤدي إلى زيادة تقدر بـ 1.9% في النمو الحضري، وبما أن النموذج يفترض أن معدلات النمو الحضري سوف تكون بنفس المعدلات الحالية تجاه العلاقة مع زيادة السكان، فهذا يعني أن النمو الحضري سيشمل في العام 2033م ما يعادل 31.5% من مجمل المساحة الحالية للمعمور الحضري.

2. يمكن أن نلاحظ أن النمو الحضري ظهر بشكل كبير في محليات أم درمان وشرق النيل وبحري، ونتيجة للحديث السابق عن أن رغبات السكن للسكان في الفترة الأخيرة قد اتجهت نحو محلية شرق النيل فإن النتيجة تعزز هذا الاتجاه في التحليل، إلا أن ارتفاع معدلات التمدد في محلية أم درمان جاء نتيجة لأن النموذج لم يعتمد على عنصر واحد في عملية التحليل، حيث جاءت الأفضلية لأم درمان نتيجة لخطوط المواصلات والطرق التي تتميز بها بالإضافة إلى إمكانية الامتداد بمجازاة النيل، كما أن المناطق المخصصة للاستخدامات غير السكنية (الزراعية والغابية) تقل في محلية أم درمان مقارنة مع بقية المحليات، مما يجعل العنصر السلبي الوحيد هو الخاص بطبيعة الأرض، أما محليات الخرطوم وجبل أولياء فإن الامتداد بها لم يكن بالحجم الكبير نتيجة لقلة المساحات غير المستقلة بها بالإضافة إلى أن هذه المناطق غير المستقلة مخصصة أصلاً لأغراض زراعية.

10. النتائج والتوصيات

10.1 النتائج

بناءً على ما تقدم من دراسة وتحليل للواقع الحالي لمدينة الخرطوم والاستراتيجيات التخطيطية وأثرها على النمو الحضري للمدينة، تم التوصل إلى عدد من النتائج وهي:
شهدت مدينة الخرطوم في تاريخها الحديث والمعاصر نمواً سكانياً ضخماً وهذا النمو مرشح للاستمرار في المستقبل حسب الإسقاطات السكانية المتوفرة، والظروف الموضوعية والتخطيطية والتنموية في البلاد.
إذا استمرت معدلات النمو بنفس الاشتراطات الحالية سوف يتمدد النمو الحضري ليشمل مناطق خارج نطاق الطريق الدائري والذي تم تحديده كحد للنمو الحضري المستقبلي للمدينة.
تحديد الطريق الدائري كحدود للمنطقة المعمورة في المخطط

الهيكلي غير مُجدٍ، خصوصاً إذا ما نظرنا إلى المنطقة الحضرية حالياً والتي تتجاوز حدود الطريق الدائري.
أظهرت نتائج الدراسة الحاجة إلى مراجعة وتحديث خطط إدارة النمو الحضري (المخططات الهيكلية) مما يحقق التنمية الحضرية المستدامة.
إن الأخذ بأسلوب التحليل المكاني يعطي إمكانيات كبيرة في بناء سيناريوهات مختلفة لما يتوفر فيه من أساليب حسابية تمكن المخطط من بناء سيناريوهات مستقبلية على أسس علمية.

10.2 التوصيات

ضرورة تحديث المخطط الهيكلي لولاية الخرطوم وتنقيحه على أسس علمية تراعي المتغيرات البشرية والمستجدات التخطيطية والتنموية للسودان ككل وولاية الخرطوم على وجه الخصوص.
تفعيل وتمكين الاعتماد على نظم المعلومات الجغرافية للمشاريع التخطيطية التنموية على مستوى المشاريع والمؤسسات العاملة في هذا المجال والتي تحتاج عملية اتخاذ القرارات التنموية بها الاعتماد على تأسيس قواعد بيانات مكانية ووصفية كبيرة ومتوسطة الحجم.
إنشاء قاعدة بيانات جغرافية مؤسسية مركزية على المستوى القومي تتوافر بها البيانات القطاعية الأساسية على الأقل والتي تنتج بمعرفة الهيئات والمؤسسات الحكومية (خرائط المساحة، خرائط المساحة الجيولوجية، بيانات الجهاز المركزي للإحصاء...الخ) مع آليات ومسئوليات للتحديث لمنع ازدواج الجهود وتقليل الوقت والجهد والتكلفة التي تتكبدها مشاريع التنمية لإعداد قواعد البيانات اللازمة لإنجاز مشروعاتها.
الاهتمام بتجهيز قاعدة من المتخصصين في تقنيات نظم المعلومات الجغرافية والاستشعار عن بعد وقواعد البيانات وتطبيقاتها في مستوى البكالوريوس والدراسات العليا لتكوين قاعدة عريضة من الكفاءات البشرية لتلبية احتياجات السوق المتزايدة واللحاق بركب هذه التقنيات عالمياً.

الخاتمة

من خلال التطبيق العملي لنموذج النمو الحضري SLEUTH المعدل على مدينة الخرطوم الكبرى اتضح

أن المخطـط الهيكلـي لولايـة الخرطـوم يحتـاج إلـى تحديـث وتنقيـح يراعـي اتجاهـات النمـو الحضـري للمدينـة ونموهـا السـكاني وخصائصهـا الطبيعيـة والبشـرية، وكذلـك ضـرورة وضـع التوسـع المسـتقبلي الطبيعـي للمدينـة فـي الحسـبان عنـد وضـع هذه المخططـات. كمـا تبيـن مـن الدراسـة الفائـدة الكبيـرة لأسـاليب التحليـل المكانـي التـي توفرهـا بيئـة برمجيـات نظـم المعلومـات الجغرافيـة فـي رسـم السياسـات التخطيطيـة المختلفة.

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scene. The prevention of SRIs can be challenging, and individualized prevention efforts should be targeted towards players. For instance, young children should be required to use appropriate ball sizes and sport devices. Furthermore, prevention efforts should target the playing field environment in order to reduce the rates of SRIs. In addition, training the teachers and coaches plays a major role in reducing SRIs. This can be achieved by enhancing their knowledge and skills in identifying risk factors for injury in each sport. These risk factors can be divided into extrinsic (such as sport place, weather, shoes) and intrinsic (such as sex, age, previous injury, body weight) causes. Teachers and coaches should monitor any modifiable risk factors for athletic health and safety, and provide directions for better playing surfaces and sports equipment that can help in the prevention of injuries.

The data provided from this study raise the awareness of SRIs for the affected players in each of these eight sports and also give hints about how important it is to formulate a sports injury prevention program. In addition, a strategic plan is needed to increase player awareness on the importance of applying safety measures while practicing sport to reduce the rate of injuries. Social media and awareness campaigns can be powerful and effective tools in educating the public and athletes in Madinah.

Further studies are required to identify injury patterns and possible relationships to popular culture events, with the ultimate goal of enabling people to safely participate in sports activities. Future research is necessary to determine the factors underlying the increase in SRIs and identify strategies for their further reductions.

CONCLUSION

Orthopedic sports related injuries are a common source of musculoskeletal trauma in Madinah. The data provided in this study raise awareness of the demand for formulating sports injury prevention programs in schools and sports facilities.

DISCLOSURE

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4.2 Importance of Findings

There have been drastic changes and developments in sports in Kingdom of Saudi Arabia. This is clear in the growth of the number of sport clubs in the country and the profound increase in the number of individuals practicing sport as a daily activity (Sadat-Ali & Sankaran-Kutty, 1985; Sadat-Ali & Sankaran-Kutty, 1987). Adolescents (10-19 years old) and young adults (20-35 years old) are most commonly engaged in sports. Moreover, Jeon *et al.* reported that the most common age groups frequently exposed to SRIs are adolescents (50%) followed by young adults (37%) (Jeon, Lee, Roh, Kim, Lee, & Lee, 2016). Despite the increase in the number of injuries, little is known about SRIs in Madinah, Kingdom of Saudi Arabia.

This study found that orthopedic sports related injuries in Madinah is a common element for patients seeking musculoskeletal medical consultation at KFH. This result agrees with a previous study by Sadat-Ali & Sankaran-Kutty (1987). Both studies show that football is the most frequent cause of SRIs in Kingdom of Saudi Arabia. In addition, the current study found that most injuries (50%) occur in patients under the age of 20 - while Sadat-Ali and Sankaran-Kutty, above, found the same age group to have a higher (63%) incidence of injury. This might be related to several factors including bone strength, not wearing protective gear while playing contact sports, poor coaching, and lack of sports guidance. Many of the injured are not professional players; they are people who are merely practicing sports for enjoyment and usually have never received any previous supervised training (Dahab & McCambridge, 2009). There were no female patients in either this study or Sadat-Ali and Sankaran-Kutty (1987), which might be attributed to the culture in Kingdom of Saudi Arabia. The study by Sadat-Ali and Sankaran-Kutty (1987) showed that musculotendinous injuries were the most common (41%) while the present study found that fractures accounted for the overwhelming majority (82%) of injuries. The knee was the most common location (27%) of injuries in the previous study but the current study found that the most common sites of injury were the wrist (40.7%) and foot (28.7%). Theoretically, this might be linked to the mechanism of injury by falling down over players' hands while running in a football match.

Several studies have investigated the nature of SRIs among youth and reported that fractures were most frequently encountered at the Emergency Departments (O'Rourke, Quinn, Mun, Browne, Sheehan, Cusack, & Molloy, 2007; Monroe, Thrash, Sorrentino, & King, 2011; Mello, Myers, Christian, Palmisciano, & Linakis, 2009). A study by Taylor and Attia (2000) determined that fractures accounted for 29.4% of all SRIs at their Emergency Unit. However, Kerr and his colleagues (Kerr *et al.*, 2015) investigated youth football related injuries in America and found that contusion, not fracture, was the most common diagnosis. Apparently, many sports participants in Madinah play without any protective gear and support. Some are untrained and others play without coaching or play in unintended positions, which might explain the diverse results between the two studies.

Despite the poor understanding of SRIs among both players and coaches, the growing trend of SRIs reported in this study may indicate an increase in the recognition and subsequent treatment of these injuries. In addition, an ever-increasing level of competitiveness and intensity of training, starting at a younger age, may be contributing to the increase in the number and degree of the severity of SRIs (Adirim & Cheng, 2003).

4.3 Strengths and Limitations

This study constitutes the first national study of SRIs for people treated by KFH-Madinah. There were some limitations, including the use of a retrospective approach in collecting and analyzing the data. In addition, the study excluded any patients who missed their follow-ups or were unreachable by phone. This undoubtedly affected the total number of patients studied. Furthermore, the estimates of this study may not be representative of SRIs treated by urgent care centers, family physicians or pediatricians, athletic trainers, physical therapists, or other sources of medical care.

4.4 Future Directions

Education among athletes is vital to address the burden of SRIs and effectively manage them. Adolescents and young adults must learn how to avoid injuries and how to deal with them at the

Table 4: Cross tabulation between sports type and anatomical location.

Sport Type	Site of Injury								Total
	Hand	Elbow	Shoulder	Humerus	Wrist	Knee	Tibia & Fibula	Foot	
Football	17	4	2	1	61	8	9	39	141
Swimming	0	0	0	1	0	0	0	0	1
Horse Riding	0	0	1	0	0	0	0	0	1
Volleyball	1	0	0	0	0	1	0	1	3
Kung Fu	0	0	0	0	0	0	0	1	1
Judo	0	0	0	0	0	0	0	1	1
Running	0	0	0	0	0	0	0	1	1
Karate	0	0	0	0	0	1	0	0	1
Total	**18**	**4**	**3**	**2**	**61**	**10**	**9**	**43**	**150**

Chi-Square Tests			
Test Types	Value	Degrees of Freedom	Asymptotic Significance (2-Sided)
Pearson Chi-Square	1.516E2[a]	49	0.000
Likelihood Ratio	36.247	49	0.912
Linear-by-Linear Association	1.390	1	0.238
No. of Valid Cases	150		

Table 5: Cross tabulation between sport type and age.

Sports Type	Age				Total
	Pediatric Group	Adolescent	Young Adult	Middle-Aged Adult	
Football	10	70	53	8	141
Swimming	0	1	0	0	1
Horse Riding	0	1	0	0	1
Volleyball	0	1	2	0	3
Kung Fu	0	1	0	0	1
Judo	0	1	0	0	1
Running	0	0	1	0	1
Karate	0	0	0	1	1
Total	**10**	**75**	**56**	**9**	**150**

Chi-Square Tests			
Test Types	Value	Degrees of Freedom	Asymptotic Significance (2-Sided)
Pearson Chi-Square	22.653[a]	21	0.363
Likelihood Ratio	14.720	21	0.837
Linear-by-Linear Association	1.753	1	0.185
No. of Valid Cases	150		

3.6 Sport Type and Type of Injury

Table (3) shows the distribution of injury type among different sports between the type of sport and type of injury. The most common type of sport leading to injury was football and the most common type of injury was a fracture. The football related injuries included 117 fractures, 10 sprains, 5 ligamentous tears, 5 dislocations, and 4 contusions. One SRI, a fracture, was related to swimming. The horse riding injury was also a fracture. The volleyball related injuries (n= 3) represented one fracture, one sprain, and one ligamentous tear. The Kung-Fu, Judo, and Running injuries were one fracture each. Lastly, the Karate related injury was a contusion.

3.7 Sports and Location

The highest number of injuries was located in the wrist (n= 61), followed by the foot (n= 39) during football. Hand injuries presented the highest rate of injuries in football (17 out of 18 patients), (Table 4).

3.8 Sports and Age

Based on the overall distribution of age groups, football injuries were seen more often in adolescents (n= 70) and young adult (n= 53), (Table 5).

4. DISCUSSION

4.1 Key Findings

The sport most commonly associated with SRIs in patients brought to KFH-Madinah was football (94%). The most frequent type of injury was fracture (82%), and the most common sites of SRIs were the wrist (40.7%) and the foot (28.7%). The most frequent age group exposed to SRIs were adolescents (50%), followed by young adults (37.3%).

Table 3: The distribution of injury type among different sports.

Sport Type	Diagnosis					Total
	Fracture	Sprain	Ligamentous Injury	Dislocation	Contusion	
Football	117	10	5	5	4	141
Swimming	1	0	0	0	0	1
Horse Riding	1	0	0	0	0	1
Volleyball	1	1	1	0	0	3
Kung Fu	1	0	0	0	0	1
Judo	1	0	0	0	0	1
Running	1	0	0	0	0	1
Karate	0	0	0	0	1	1
Total	123	11	6	5	5	150

Chi-Square Tests			
Test Types	Value	Degrees of Freedom	Asymptotic Significance (2-Sided)
Pearson Chi-Square	40.607[a]	28	0.058
Likelihood Ratio	14.487	28	0.983
Linear-by-Linear Association	4.100	1	0.043
No. of Valid Cases	150		

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Table 1: Sport specific types sorted by number of injuries.

Sports Type	Frequency	Percent (%)	Cumulative Percent (%)
Football	141	94.00	94.0
Swimming	1	0.70	94.7
Horse Riding	1	0.70	95.3
Volleyball	3	2.00	97.3
Kung Fu	1	0.70	98.0
Judo	1	0.70	98.7
Running	1	0.70	99.3
Karate	1	0.70	100.0
Total	**150**	**100.0**	

3.2 Age

A variety of age groups were represented; the youngest patient was 6 years old and the oldest was 55 years. The overall distribution of age groups showed that the majority of sport injuries (50%; n= 75) were in the adolescent age group, followed by young adults (37.3%; n= 56), pediatric patients (6.7%; n= 10), and middle-aged adults (6%; n= 9), (Figure 1).
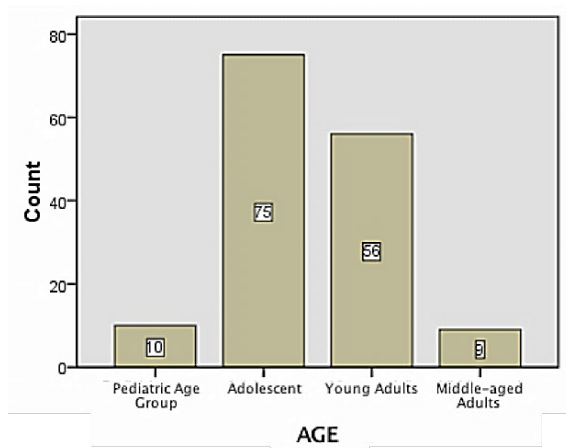

Figure 1: Bar graph showing the frequency of sport injury among different age groups.

3.3 Nationality

The total number of patients according to their nationality (Saudi or Non-Saudi) dramatically showed that more SRI patients were Saudi (90.7%; n= 136) than non-Saudi patients (9.3%; n= 14).

3.4 Types of Injury

Patients presented with multiple types of injuries. These injuries were categorized into five types of SRIs (diagnosis), including: fractures, sprains, ligamentous tears, dislocations, and contusions (Table 2). The results showed that injuries consisted primarily of fractures (82%; n= 123), followed by sprains (7.3%; n= 11). These were followed by ligamentous tears (4%) and then dislocations and contusions (3% each).

Table 2: Sports injury specific diagnosis sorted by number of injuries.

Sports Injury Type	Frequency	Percent (%)	Cumulative Percent (%)
Fracture	123	82.00	82.0
Sprain	11	7.30	89.3
Ligamentous Tear	6	4.00	93.3
Dislocation	5	3.30	96.7
Contusion	5	3.3	100.0
Total	**150**	**100.00**	

3.5 Site of Injury

SRIs were encountered in eight major anatomical locations, including: hand, elbow, shoulder, humerus, wrist, knee, tibia and fibula, and foot. The most frequent sites of injuries were the wrist (40.7%) and the foot (28.7%), followed by hand (12%), knee (6.7%), tibia and fibula (6%), elbow (2.7%), shoulder (2%), and humerus (1.3%), (Figure 2).
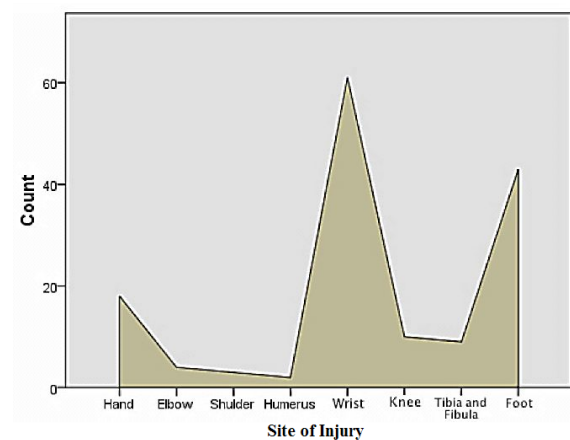

Figure 2: Area chart describing the anatomical location of the sport injury.

1. INTRODUCTION

Nowadays, sport is a daily activity for all age groups, including almost all children and adolescents. As there is an increase among people engaging in sporting exercises or games, this will naturally accompany a parallel increase in the numbers of sport injuries. A sport related injury (SRI) is defined as damage that results from sudden trauma or recurrent stress accompanying an athletic activity. These injuries may affect bones or soft tissues such as ligaments, muscles, and tendons (Timpka, Jacobsson, Bickenbach, Finch, Ekberg, & Nordenfelt, 2014).

Sport related injuries are a common cause of morbidity and their treatment is difficult, expensive, and time-consuming. Unfortunately, SRIs more commonly affect young adults and may result in life-long damage that negatively affects community productivity (Goldberg, Moroz, Smith, & Ganley, 2007; Adirim & Cheng, 2003). Researchers reviewed the SRI cases in British Columbia Children's hospital between 1992 and 2005. Their results showed a significant increase in SRIs in the pediatric age population, with a 28% increase in the number of injuries that result from sports activity (Pakzad-Vaezi & Singhal, 2011). As the number of injuries resulting from sport continues to increase, the likelihood of sustaining an injury needs to be elucidated. Furthermore, several studies have reported higher injury rates for boys, but more severe injuries for girls. However, it remains unclear whether sex differences as males or females correlate with specific types of sports injuries and how these injuries vary by sport (Yaniv & Sever, 2015; Kerr, Marshall, Simon, Hayden, Snook, Dodge, Gallo, Valovich McLeod, Mensch, Murphy, & Nittoli, 2015).

Almadinah Almunawwarah (Madinah) is one of the largest provinces in Kingdom of Saudi Arabia, with a population exceeding 1.5 million. King Fahad Hospital (KFH) is the tertiary health care and trauma center covering the whole region. The purpose of this study was to identify the most common types of sports that lead to admission for injury at KFH, Madinah, and analyze the relationship of these injuries with different variables including patients' age, sex, nationality, site of the injury, and type of injury.

2. PATIENTS AND METHODS

2.1 Patient Inclusion and Data Collection

Hospital Research and Ethics Board approval was obtained. A retrospective review of the orthopedic database at this institution from January 2010 to December 2015 was performed to identify all patients with sport related injuries. Any case that involved a motor vehicle accident or non-sport related fall was excluded. Detailed clinical information was collected from patient's medical records. In addition, patients were contacted by phone to obtain further details about the injury. All information about the nature of the injury, age of patient at time of injury, site of injury, and type of sport that led to injury were recorded. The patients' age groups were classified as follows: children patients were less than 10 years old, adolescents between 10 and 19 years, young adults between 20 and 35 years, middle-aged adults ranged between 36 and 55 years.

2.2 Statistical Analysis

A descriptive statistical analysis was performed for each variable. All statistical tests were conducted with the Statistical Package of Social Sciences (SPSS) version 16.0 (SPSS Inc, Chicago, IL, USA). Significance was set at p-value < 0.05.

3. RESULTS

A review of the orthopedic database at KFH-Madinah identified a total of 150 patients with injuries related to sport activities. The majority were Saudi citizens (n= 146). Moreover, the most common type of sport that led to injuries was football (94%; n= 141). The most frequent type of injury was fracture (82%; n= 123), with 117 fractures resulting from football alone. Furthermore, this study revealed that the most common sites of injuries are the wrist (40.7%) and the foot (28.7%). The majority of cases were found in adolescents (50%), followed by young adults (37.3%).

3.1 Types of Sport

The SRI patients (n= 150) were divided into the type of sport, as shown in Table (1). The most popular sport in Madinah is football (94%; n= 141), followed by volleyball (2%; n= 3). Other sports included Swimming, Horse riding, Kung Fu, Judo, Running, and Karate.

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تقييم الإصابات الرياضية في المدينة المنورة ـ المملكة العربية السعودية

عبدالملك الملا[1]، عبدالله سنبل[1]، ثبات الفريدي[1]، يسر دبور[1]، رائد أبو طالب[2]، بندر حتيمش[3]*

ملخص البحث: هدفت هذه الدراسة إلى إلقاء الضوء على الإصابات الرياضية الشائعة في مستشفى الملك فهد بالمدينة المنورة ـ المملكة العربية السعودية، وتحليل علاقتها بالمتغيرات الشخصية والتشريحية للمريض. الطرق: مراجعة بأثر رجعي لبيانات مرضى الإصابات الرياضية للفترة من يناير 2010م إلى ديسمبر 2015م لمدة ستة أشهر كحد أدنى للمتابعة. يتم تسجيل بيانات طبيعة ومكان الإصابة، عمر المريض، ونوع الرياضة المتسببة بالإصابة، وحيث تم التوصل الى 150 مريض. النتائج توضح أن كرة القدم هي الرياضة الأكثر تسببا للإصابات الرياضية (94%)، الكسور هي الإصابة الأكثر شيوعا في مركزنا (82%)، الكسور الناتجة عن رياضة كرة القدم تشكل (83%) من نسبة الإصابات. وجد أن إصابات مفصل الرسغ (40%) والقدم (28%) هي الأكثر انتشارا بين الحالات. كما وجد أن غالبية الإصابات هي في سن المراهقة (50%). الاستنتاجات: هناك تزايد لأعداد الإصابات الرياضية عند اليافعين في مركزنا. نتائج هذه الدراسة تدعو الى صياغة برامج مكافحة مستقبلية للتوعية بالإصابات الرياضية في المدارس والمرافق الرياضية.

الكلمات المفتاحية: الرياضة؛ إصابة؛ المدينة المنورة؛ المملكة العربية السعودية.

* للمراسلة:

(1) كلية الطب، جامعة طيبة، المدينة المنورة 344، ص.ب. 30001، المملكة العربية السعودية.

(2) قسم جراحة العظام، مستشفى الملك فهد، المدينة المنورة 2141، ص.ب. 378، المملكة العربية السعودية.

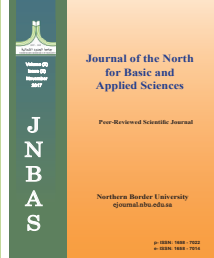(3)* قسم جراحة العظام، كلية الطب، جامعة جدة، جدة 80327، ص.ب. 21589، المملكة العربية السعودية.

e-mail: dr_hetaimish@hotmail.com

EVALUATION OF SPORTS RELATED INJURIES
IN ALMADINAH ALMUNAWWARAH,
KINGDOM OF SAUDI ARABIA

Abdulmalek Almulla[1], Abdullah Sonbol[1], Thabat Alfraidi[1], Yosor Dabbour[1],

Raid A. Abutalib[2], Bandar Hetaimish[3*]

Abstract: The purpose of this study was to identify the most common types of sports injuries treated at King Fahad Hospital, Madinah, Kingdom of Saudi Arabia and analyze their relationship with demographic and anatomical variables. Methods: a retrospective review of an orthopedic database from January 2010 to December 2015 was performed to identify patients with sports related injuries. Data about the nature of the injury, age of patient at time of injury, site of injury, and type of sport that lead to orthopedic injury were recorded. Results: The study identified 150 male patients. The most common type of sport that led to injury was football (94%; n= 141), and the most common type of injury was fracture (82%; n= 123). Fractures that resulted from football injuries represented 117 cases (83%). The study revealed that the most common injury sites were the wrist (40%) and the foot (28%). The majority of cases were found in adolescents (50%), followed by young adults (37%). Conclusions: Orthopedic sports related injuries are common sources for musculoskeletal trauma in Almadinah Almunawwarah (Madinah). The data provided from this study raise an awareness of the demand for formulating sports injury prevention programs in schools and sports facilities.

* Corresponding Author:

(1) College of Medicine, Taibah University, Almadinah Almunawwarah 30001, P.O.Box 344, Kingdom of Saudi Arabia.

(2) Departments of Orthopedic Surgery, King Fahd Hospital, Almadinah Almunawwarah 2141, P.O.Box 378, Kingdom of Saudi Arabia.

(3)* Department of Orthopedic Surgery, Medical College, University of Jeddah, Jeddah 21589, P.O.Box 80327, Kingdom of Saudi Arabia.

e-mail: dr_hetaimish@hotmail.com

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docking studies of already reported and established benzimidazole derivatives which have already been screened for other types of biological activities. This may also result in the identification of a safe, potent, and efficacious benzimidazole derivative as an angiotensin receptor antagonist.

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3. DISCUSSION

The Renin Angiotensin System (RAS) is implicated in the pathogenesis of hypertension. Three types of antihypertensive drugs are used that affect this system. These are renin inhibitors, for example, aliskiren, remikiren, enalkiren, and zankiren; Angiotensin Converting Enzyme (ACE) inhibitors, such as lisinopril, captopril, enalapril, ramipril, and fosinopril; and angiotensin II receptor antagonists, for example, losartan, valsartan, irbesartan, telmisartan, olmesartan, and candesartan. Recently, benzimidazole derivatives have emerged as an important scaffold for the development of angiotensin II receptor antagonists as antihypertensive agents. Some of these benzimidazole derivatives, for example, candesrtan, telmisartan, and azilsartan, have already been approved by the USFDA for the treatment of hypertension and related cardiac conditions. Based on the relationship between the AT_1 receptor and blood pressure regulation as well as the structure activity relationship studies of benzimidazole derivatives, newer benzimidazole derivatives as the AT_1 receptor antagonists are being developed for the treatment of hypertension. This is evident by the filing of recent patent applications related to benzimidazole derivatives as AT_1 receptor antagonists, such as United States Patent Application Number 20120172401 A1, United States Patent Application Number 20090054502 A1, PCT Publication Number WO 2009/076288 A1, PCT Publication Number WO 2008/153857 A1, PCT Publication Number WO 2004/082621 A1, Russian Patent Number 0002501798, Chinese Patent Publication Number 102276534, and Japan Patent Application Number 2011101381. It has been suggested by researchers that the alkyl group at C-2 position of benzimidazole moiety is essential for lipophilic interaction with the receptor and an ionized acidic group, such as a tetrazole or carboxyl group, on biphenyl moiety is responsible for ionic interaction with the AT_1 receptor (Vyas & Ghate, 2010; Bergsma, Ellis, Kumar, Nuthulaganti, Kersten, Elshourbagy, Griffin, Stadel, & Aiyar, 1992; Underwood, Strader, Rivero, Patchett, Greenlee, & Prendergast, 1994; Carini, Duncia, Aldrich, Chiu, Johnson, Pierce, Price, Snatella, Wells, Wexler, Wong, Yoo, & Timmermans, 1991; Kubo, Yasuhisa, Imamiya, Yoshihiro, Inada, Furukawa, & Nishikawa, 1993; Ries, Mihm, Narr,

Hasselbach, Wittneben, Entzeroth, Van Meel, Wienen, & Hauel, 1993). The N-3 of benzimidazole is likewise important as it also interacts with these receptors through hydrogen bonding. Besides these essential features, other possible variations have also been reported by the researchers mentioned above. A carboxyl group at C-7 position, a small alkoxy group at C-2 position, and an acylamino group at C-6 position of benzimidazole nucleus have been reported for better AT_1 receptor antagonistic activity. Accordingly, scientists are working to develop newer AT_1 receptor antagonists that contain a benzimidazole nucleus with emphasis in order to maintain their potency, duration of action, and bioavailability.

CONCLUSION & RECOMMENDATION

It is evident from the literature, that benzimidazole derivatives are an important scaffold for the development of clinically used drugs. Many researchers and scientist have published and established important structure activity relationship studies related to the diverse pharmacological activities of this chemical moiety. A complete knowledge and understanding of the structure activity relationship studies of benzimidazole derivatives as angiotensin receptor antagonists is helping the scientist to develop a novel benzimidazole derivative as angiotensin receptor antagonists. In this review, the authors have tried to highlight the potential development of novel benzimidazole derivatives as AT_1 receptor antagonists that may be helpful to the medicinal chemist fraternity for a target oriented and comprehensive information. Further, it would be interesting to see how many newer benzimidazole derivatives will be able to see the light of future as approved drugs for the treatment of hypertension.

Keeping in mind the potential of benzimidazole derivatives as an important scaffold for the development of newer angiotensin receptor antagonists for the treatment of hypertension. It is recommended to design, synthesize, and develop newer molecules containing this chemical moiety as angiotensin receptor antagonists. It is also recommended to perfom *in silico* toxicity studies, drug likeliness prediction studies, and molecular
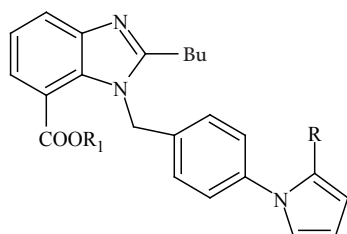
(19) R = Tetrazole; R_1 = -Me
(20) R = -COOH; R_1 = H

Figure 24: The chemical structure of the compounds 19 & 20.

Substituted carboxamido benzimidazole derivatives with C-5 amino group on benzimidazole nucleus with different alkyl or aryl carbonyl chains as AT_1 antagonists were developed (Shah, Sharma, Bansal, Bansal, & Singh, 2008). It was observed that the compounds 21-24 (Figure 25) were non-competitive antagonists, whereas the compounds 25-27 (Figure 25) were competitive antagonists. It was also suggested that a methyl group can be accommodated in the AT_1 receptor pocket, that a suitable alkyl group may increase the antihypertensive activity, and that an increase in the bulk of the alkyl or aryl moieties retards the activity.
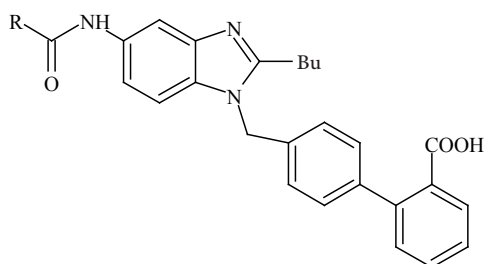
(21) R = -Me; **(22)** R = Et; **(23)** R = -nPr; **(24)** R = -nBu;
(25) R = -Ph; **(26)** R = 2-ClPh; **(27)** R = 2-ClPh

Figure 25: The chemical structure of the compounds 21-27.

The 5-sulfamoyl benzimidazole derivatives as AT_1 receptor antagonists have been reported (Kaur, Kaur, Bansal, Shah, Bansal, & Singh, 2008). This series of compounds was based on isosteric replacement of the nitro group at C-5 of benzimidazole moiety with a sulfonyl group that was further extended with appropriate alkylamino group. It was suggested that the sulfonyl group mimics the nitro group, that the

alkylamino may interact with the H-bond acceptor group, and that the alkyl group (R) may form a stronger drug-receptor complex. It was shown that the tert-butylsulfamoyl analog 28 (Figure 26) has the maximum antagonistic activity during *in vitro* studies, but that the cyclohexyl-sulfamoyl analog 29 (Figure 26) has the maximum decrease in MABP in hypertensive rats.
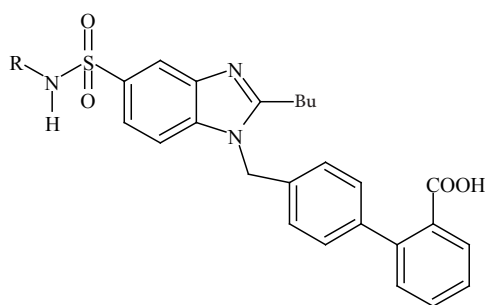
(28) R = *tert*-Bu **(29)** R = cyclohexyl

Figure 26: The chemical structure of the compounds 28 & 29.

Some benzimidazoles have been synthesized by replacing the tetrazole ring of biphenyl moiety with imidazole, 5- chloroimidazole, 1,2,4-triazol and imidazoline ring system with an additional methyl benzimidazole moiety at C-6 of benzimidazole (Guo, Lin, Rui, Xiao-Xiao, Bo-Gang, & Xiao-Xia, 2008). These compounds were subjected for their AT_1 receptor antagonistic activity. The *in vitro* and *in vivo* results revealed that imidazoline derivative 30 (Figure 27) having an IC50 value of 2.6 x 10-7 μM had an almost equipotent activity to that of telmisartan.
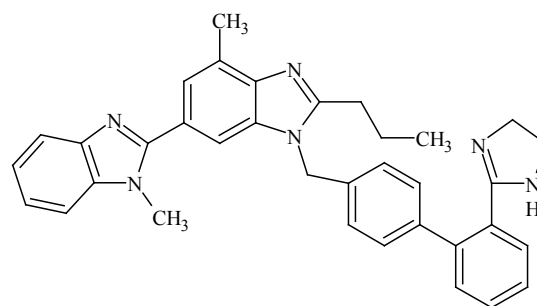

Figure 27: The chemical structure of the compound 30.

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binding with the AT$_1$ receptor having IC$_{50}$ value of of 1.7 μmol. The compound 13 (Figure 20) having an IC$_{50}$ value of 1.6 μmol was found to have a better affinity to the receptor than pimobendan.
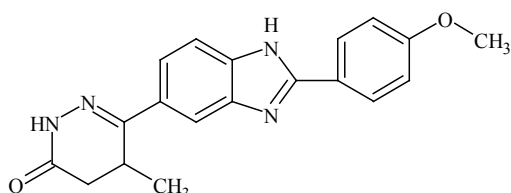

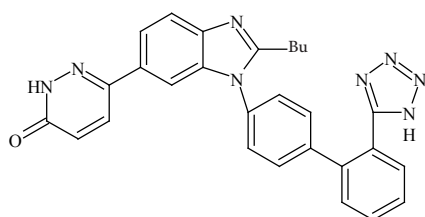**Figure 19: The chemical structure of pimobendan.**

Figure 20: The chemical structure of the compound 13.

A research group (Palkowitz, Steinberg, Zimmerman, Thrasher, Hauser, & Boyd, 1995) reported a series of 5-aryl benzimidazole derivatives, wherein the compound 14 (Figure 21) was obtained as the most potent AT$_1$ receptor antagonist.
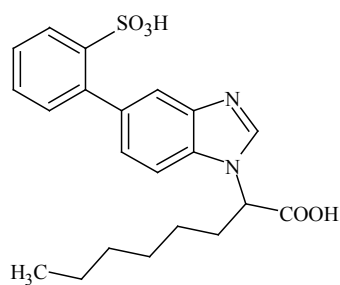

Figure 21: The chemical structure of the compound 14.

A study of 5-nitrobenzimidazole derivatives (Bali, Bansal, Sugumaran, Saggu, Balakumar, Kaur, Bansal, Sharma, & Singh, 2005) describes the synthesis of substituted benzimidazole by varying substitutions on C-2 of benzimidazole ring. These compounds were designed by a computer aided drug design with respect to losartan with the expectation

of having more potent AT$_1$ receptor antagonists. The study concluded that the compound 15 (Figure 22) having the nitro group at C-5 and n-butyl side chain at the C-2 of benzimidazole moiety was more potent than candesartan.
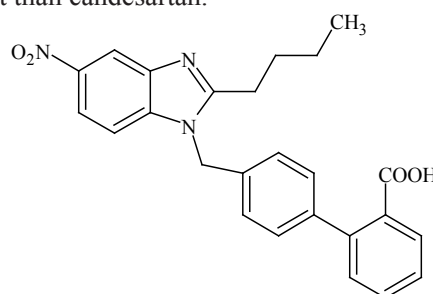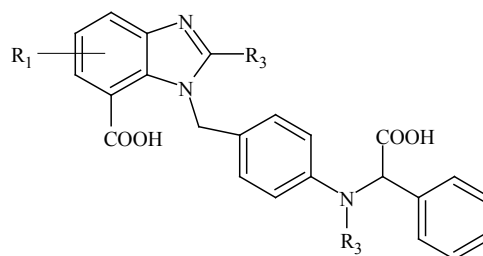

Figure 22: The chemical structure of the compound 15.

A series of benzimidazoles, wherein biphenyl tetrazole moiety was replaced by (phenylamino) phenylacetic acid moiety has been reported (Xu, Ran, Hua, Wu, Wang & Zhang, 2007). The synthesized compounds were subjected for their AT$_1$ antagonistic activity and it was revealed that the compounds 16-18 (Figure 23) exhibited potent antagonistic activity of the AT$_1$ receptor that was higher than losartan.

(16) R$_1$ = 5-OMe; R$_2$ = -Bu; R$_3$ = -Me
(17) R$_1$ = H; R$_2$ = -Bu; R$_3$ = -Et
(18) R$_1$ = 6-OMe; R$_2$ = -Bu; R$_3$ = -Me

Figure 23: The chemical structure of the compounds 16-18.

Similarly, the biphenyl tetrazole moiety was replaced with phenylpyrole tetrazole moiety in a series of 2-alkyl benzimidazoles (Xu *et al.*, 2007). The synthesized compounds were subjected for their ability to be potentially competitive AT$_1$ receptor antagonist. The results revealed that this bioisosteric replacement produced extremely potent compounds 19 and 20 (Figure 24).
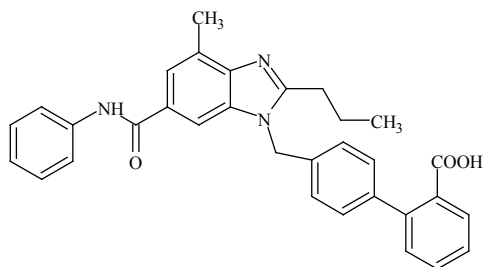
Figure 14: The chemical structure of the compound 3.

A series of benzimidazole derivatives bearing sulfonamide group was synthesized and tested for their antihypertensive activity with respect to losartan (Figure 15) (Bai, Wei, Liu, Xie, Yao, Wu, Jiang, Wang, & Xu, 2012). The compound 4 (Figure 16) was identified as the most active compound (IC_{50} = 8.5 nM) that antagonized AT_1 receptor and showed more potency than losartan (IC_{50} = 95 nM).
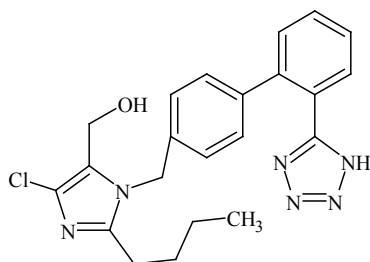

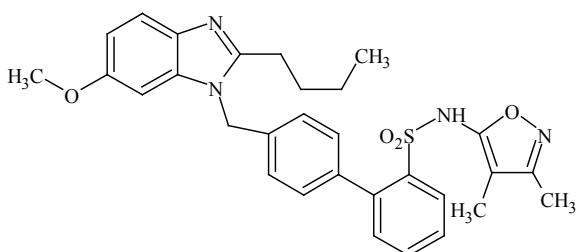**Figure 15: The chemical structure of Losartan.**

Figure 16: The chemical structure of the compound 4.

Wang *et al*. reported a series of 6-substitutedaminocarbonyl benzimidazoles as nonpeptidic AT_1 receptor antagonists (Wang, Zhang, Zhou, Li, Xue, Xu, Hao, Han, Fei, Liu, & Liang, 2012). The preliminary screening revealed that all compounds of this series were potent, whereas the compound 5 (Figure 17) was found to be an orally

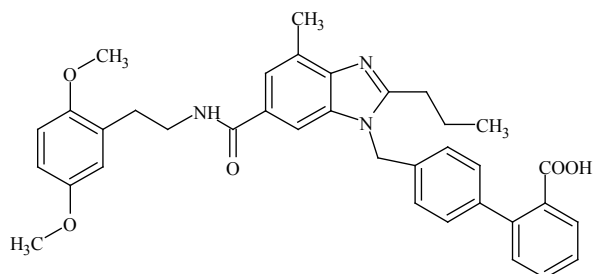active, potent AT_1 receptor antagonist with a low toxicity; this requires further investigation.

Figure 17: The chemical structure of the compound 5.

A study focused on the replacement of the tetrazole moiety by other acidic groups to improve the oral bioavailability and also solve the synthetic and metabolic problems has been performed (Kohara, Kubo, Imamiya, Inada, & Naka, 1996). The reported benzimidazole 7-carboxylic acids containing acidic heterocyclic rings as novel tetrazole bioisostreres were checked for their AT_1 antagonistic activity, wherein the biososteres of tetrazole compounds of chemical formula 6-11 were found more potent than their tetrazole counterpart of chemical formula 12 (Figure 18).
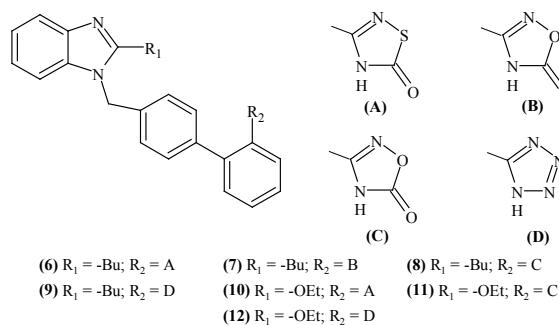

(6) R_1 = -Bu; R_2 = A   **(7)** R_1 = -Bu; R_2 = B   **(8)** R_1 = -Bu; R_2 = C
(9) R_1 = -Bu; R_2 = D   **(10)** R_1 = -OEt; R_2 = A   **(11)** R_1 = -OEt; R_2 = C
(12) R_1 = -OEt; R_2 = D

Figure 18: The chemical structure of the compounds 6-12.

Novel (6-oxo-3-pyridazinyl)-benzimidazole derivatives obtained by the derivatization of pimobendan have been prepared as AT_1 receptor antagonists (Dorsch, Mederski, Beier, Lues, Minck, & Schelling, 1994). Pimobendan (Figure 19), an inhibitor of phosphodiesterase III showed significant
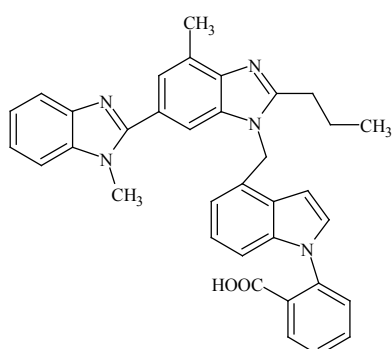
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Figure 10: The chemical structure of 2-[4-[[2-n-propyl-4-methyl-6-(1-methylbenzimidazol-2-yl)benzimidazole-1-yl]methyl]-1H-indol-1-yl]benzoic acid.

Some AT$_1$ blockers having 6-substitutedcarbamoylbenzimidazoles were evaluated for their ability to displace [(125)I] Sar(1) Ile(8)-Ang II, which was specifically bounded to the AT$_1$ receptor (Han, He, Wang, Xu, Hao, Liang, Zhang, & Zhou, 2015). The radio ligand binding assays showed that several compounds have a nanomolar affinity for the AT$_1$ receptor. It was also observed that the IC$_{50}$ values of some compounds for binding with AT$_1$ receptor were comparable with Losartan (IC$_{50}$ = 28.6 nM). The compound 1 (Figure 11) having IC$_{50}$ value of 1.1 nM was identified as a lead compound with good AT$_1$ receptor antagonistic activity and low toxicity.
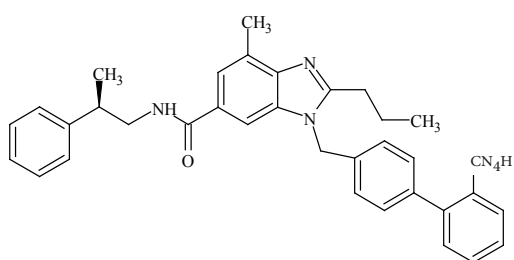

Figure 11: The chemical structure of the compound 1.

A series of 5-nitrobenzimidazoles as ARB has been reported (Zhu, Da, Wu, Zheng, Zhu, Wang, Yan, & Chen, 2014). The compound, 2-(4-((2-butyl-5-nitro-1H-benzo[d]imidazol-1-yl)methyl)-1H-indol-1-yl) benzoic acid (Figure 12), exhibited a high affinity for the angiotensin II type 1 receptor with IC$_{50}$ value of 1.03±0.26 nM. It was concluded that this compound could be an effective and durable anti-

hypertensive agent and must be further investigated for its therapeutic benefits.
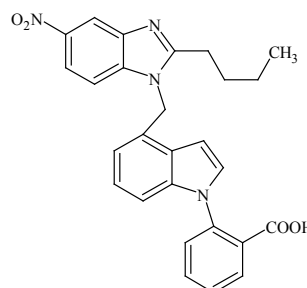

Figure 12: The chemical structure of 2-(4-((2-butyl-5-nitro-1H-benzo[d]imidazol-1-yl)methyl)-1H-indol-1-yl)benzoic acid.

A novel series of substituted benzimidazoles was designed and its ADMET (absorption, distribution, metabolism, excretion and toxicity) was predicted using in silico methods (Vyas, Gupta, Ghate, & Patel, 2014; Vyas, Ghate, Chintha, & Patel, 2013). It was reported that some key features in substituted benzimidazole derivatives, such as lipophilicity and H-bonding at the 2- and 5-positions of the benzimidazole nucleus, respectively, for the AT$_1$ receptor antagonistic activity play an important role.

A series of 6-substitutedaminocarbonyl as well as acylamino benzimidazoles was prepared as nonpeptidic AT$_1$ receptor antagonists (Zhang, Wang, Yu, Zhou, Tao, Wang, Xue, Xu, Hao, Han, Fei, Liu, & Liang, 2013). Some compounds showed good binding affinity for the AT$_1$ receptor. Two compounds of this series, namely compound 2 (AT$_1$ IC$_{50}$ = 3 nM, AT$_2$ IC$_{50}$ > 10,000 nM, PA$_2$ = 8.51) (Figure 13) and compound 3 (Figure 14) (AT$_1$ IC$_{50}$ = 0.1 nM, AT$_2$ IC$_{50}$ = 149 nM, PA$_2$ = 8.43) displayed good antagonistic activity with the additional advantage of being orally active.
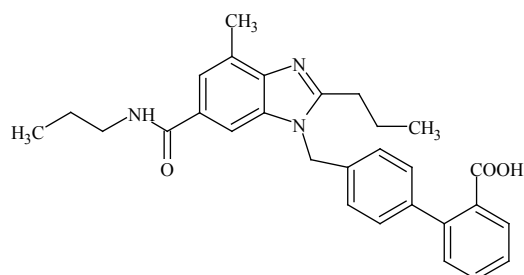

Figure 13: The chemical structure of the compound 2.

2.1.2 Telmisartan

Telmisartan (MICARDIS) (Figure 7) is a non-peptide AT_1 receptor antagonist. It was approved by the US FDA for the treatment of hypertension on April 4, 2000 and was first disclosed in the European Patent Number 0502314 B1. Telmisartan is chemically described as 4'-[(1,4'-dimethyl-2'-propyl [2,6'-bi-1H-benzimidazol]-1'-yl)methyl]-[1,1'-biphenyl]-2-carboxylic acid and is available as tablets for oral administration, containing 20 mg, 40 mg or 80 mg of telmisartan (Bakheit, Abd-Elgalil, Mustafa, Haque, & Wani, 2015; Frampton, 2011; Destro, Cagnoni, Dognini, Galimberti, Taietti, Cavalleri, & Galli, 2011).
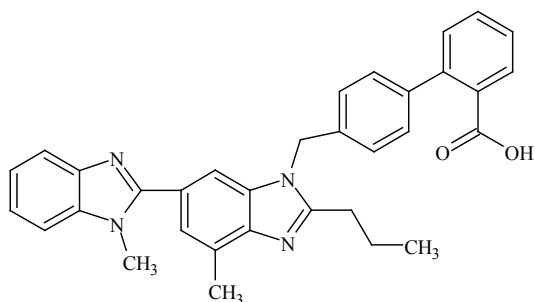

Figure 8: The chemical structure of Azilsartan medoxomil.

Figure 7: The chemical structure of Telmisartan.

2.1.3 Azilsartan medoxomil

Azilsartan medoxomil (EDARBI) (Figure 8), a prodrug, is hydrolyzed to azilsartan (Figure 9) in the gastrointestinal tract during absorption, which is a selective AT_1 receptor antagonist. It is also known as azilsartan kamedoxomil as it is marketed as a potassium salt and has the chemical name as (5Methyl-2-oxo-1,3-dioxol-4-yl)methyl-2-ethoxy-1-{[2'-(5-oxo-4,5-dihydro-1,2,4-oxadiazol-3-yl) biphenyl-4yl]methyl}-1H-benzimidazole-7-carboxylate monopotassium salt. This drug was first disclosed in the United Patent Number 7,157,584 B2. Edarbi was approved by the USFDA for the treatment of hypertension on February 25, 2011 and is available for oral use as tablets which contain 42.68 or 85.36 mg of azilsartan kamedoxomil equivalent to 40 mg or 80 mg, respectively, of azilsartan medoxomil (Angeloni, 2016; Perry, 2012; Zaiken & Cheng, 2011).
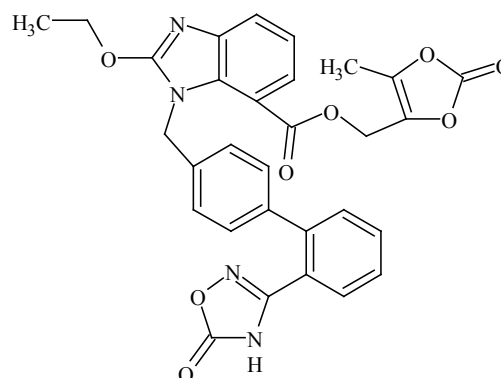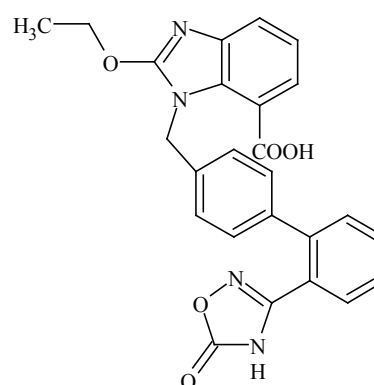

Figure 9: The chemical structure of Azilsartan (TAK-536).

2.2 Recent Benzimidazole Derivatives as Angiotensin II Receptor Antagonist

The *in vitro* and *in vivo* activity evaluation of 6-substitutedbenzimidazoles as angiotensin II receptor antagonists are described (Zhu, Bao, Ren, Da, Wu, Li, Yan, Wang, & Chen, 2016). Many synthesized benzimidazoles exhibited high affinities for AT_1 receptor when compared with telmisartan. The compound 2-[4-[[2-n-propyl-4-methyl-6-(1-methylbenzimidazol-2-yl)benzimidazole-1-yl] methyl]-1*H*-indol-1-yl]benzoic acid (Figure 10) was found to cause a significant decrease in blood pressure. The toxicity study of this compound revealed that this had a low acute toxicity and further studies have been recommended for its therapeutic application.

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omeprazole, esomeprazole, lansoprazole, dexlansoprazole, pantoprazole, and rabeprazole (proton pump inhibitor); pimobendan (cardiotonic agent); lobendazole, mebendazole, oxibendazole, albendazole, thiabendazole, and oxfendazole (anthelmintic agent); enviroxime and enviradine (antiviral agent); bendamustine, veliparib, dovitinib, (anticancer agent).

In 2010, Vyas and Ghate reviewed benzimidazole derivatives as antagonists of AT_1 receptor (Vyas & Ghate, 2010). They highlighted some important benzimidazole derivatives, such as telmisartan, candesartan, TCV-116, CV-11974 (Figure 2), CV-11194 (Figure 3), BIBR-277 (Figure 4), and TAK-536 as AT_1 receptor antagonist.
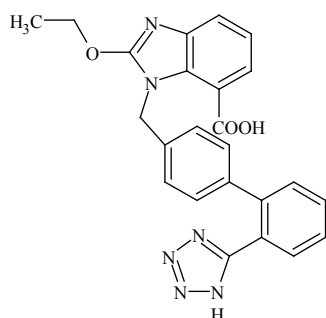

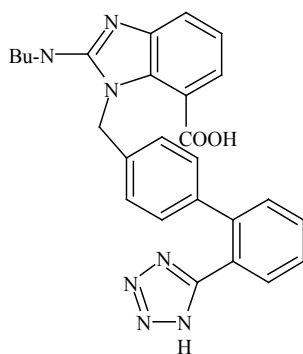**Figure 2: The chemical structure of CV-11974.**

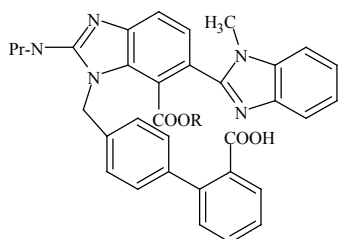**Figure 3: The chemical structure of CV-11194.**

Figure 4: The chemical structure of BIBR-277.

2.1 US FDA Approved Benzimidazole Derivatives as Angiotensin II Receptor Antagonists

2.1.1 Candesartan cilexetil

Candesartan cilexetil (ATACAND) (Figure 5), a prodrug of candesartan (Figure 6), was approved by the US FDA on Jun 4, 1998 and was first disclosed in the United States Patent Number 5,196,444. The chemical name of this drug is (±)-1-Hydroxyethyl 2-ethoxy-1-[p-(o-1H-tetrazol-5ylphenyl)benzyl]-7-benzimidazolecarboxylate, cyclohexyl carbonate (ester). Candesartan cilexetil is a racemic mixture containing one chiral center at the cyclohexyloxycarbonyloxy ethyl ester group. Following an oral administration, candesartan cilexetil undergoes hydrolysis at the ester link to form the active drug, candesartan, which is achiral. It is a selective AT_1 receptor antagonist that is indicated for the treatment of hypertension and is available for oral use as tablets containing either 4 mg, 8 mg, 16 mg, or 32 mg of candesartan cilexetil (Ardiana, Lestari, & Indrayanto, 2012; Joost, Schunkert, & Radke, 2011).
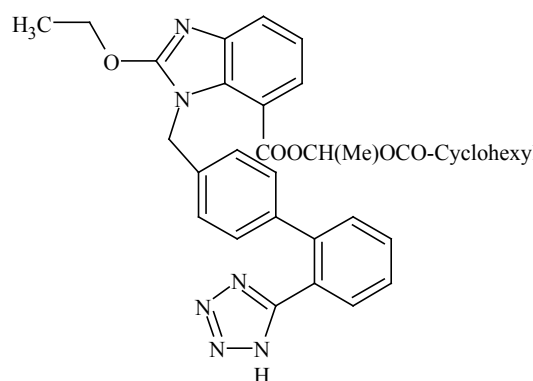

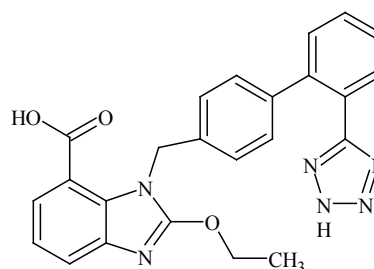**Figure 5: The chemical structure of Candesartan cilexetil (TCV-116).**

Figure 6: The chemical structure of Candesartan.

1. INTRODUCTION

Hypertension is a major cause of death worldwide as well as one of the main causes of death in the Saudi population (Imran & Abida, 2016; Gaetano, 2013; Al-Sieni, Baghdadi, & Al-Abbasi, 2014). This disease is no longer an old age disease as it is also affecting adults and children. Accordingly, it has been recommended to establish well-equipped hospitals for the care of hypertensive children in many countries, including the Kingdom of Saudi Arabia (Al-Mendalawi, 2010). Researchers have also advised that there is a need for further research in the field of hypertension as the prevalence of this disease is increasing in all age groups throughout the world (Temilolu & Miller, 2009; Reddy, 2002). Therefore, researchers have started exploring new approaches for the treatment of hypertension (Oparil & Schmieder, 2015). The current treatment of hypertension that involves the use of drugs belonging to the class of Angiotensin-converting enzyme Inhibitors (ACEIs), Angiotensin Receptor Blockers (ARBs), Thiazide and Thiazide-like Diuretics, Calcium Channel Blockers (CCB), β-Blockers, α-Blockers, Centrally Acting Agents, Direct Vasodilators, and Mineralocorticoid Receptor Antagonists (Weber, Schiffrin, White, Mann, Lindholm, Kenerson, Flack, Carter, Materson, Ram, Cohen, Cadet, Jean-Charles, Taler, Kountz, Townsend, Chalmers, Ramirez, Bakris, Wang, Schutte, Bisognano, Touyz, Sica, & Harrap, 2014). The ACEIs and ARBs act by interfering with the renin angiotensin system (RAS), which is implicated in the pathogenesis of hypertension (Naik, Murumkar, Giridhar, & Yadav, 2010). The renin angiotensin system (RAS) is a hormonal cascade which produces angiotensin peptides. The circulating renin converts angiotensinogen to Angiotensin I, which is rapidly converted to Angiotensin II by the action of Angiotensin Converting Enzyme (ACE). Angiotensin II causes vasoconstrictor through its interaction with the AT_1 receptor. Therefore, drugs that prevent the generation of Angiotensin II from Angiotensin I by inhibiting the enzyme Angiotensin Converting Enzyme (ACE) as well as Angiotensin Receptor Blockers (ARBs), are clinically used as antihypertensive agents, for example, captopril, enalapril and Lisinopril (ACE inhibitors) and telmisartan, candesartan, olmesartan and azilsartan (ARBs) (Naik *et al.*, 2010).

Telmisartan, candesartan, olmesartan and azilsartan are benzimidazole derivatives, potent ARBs, that are approved by the FDA and commonly used for the management of hypertension. This review highlights the development of recent and important benzimidazole derivatives as potential angiotensin II, Type-I (AT_1) receptor antagonists that may be able to see the light of the future as approved drugs for the treatment of hypertension.

Initially, the medicinal importance of the core structure of benzimidazole and various related groups of drugs are mentioned briefly. Then, the structure-activity relationship of benzimidazole derivatives approved by the US FDA for the treatment of hypertension is described, followed by a rather comprehensive review of newer benzimidazole derivatives that are angiotensin receptor antagonists and have the potential for the development of antihypertensive drugs.

2. BENZIMIDAZOLE DERIVATIVES AS ANGIOTENSIN RECEPTOR ANTAGONISTS

Benzimidazole has the following general formula (Figure 1) and this heterocyclic moiety has an important place in medicinal chemistry (Wright, 1951).
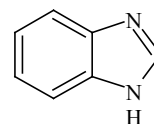
Figure 1: General structure of benzimidazole.

Many review articles have been published that provide the importance of benzimidazole derivatives in medicinal chemistry and their role in the development of medicinal compounds for clinical use (Rajasekhar, Maiti, Balamurali, & Chanda, 2017; Ajani, Aderohunmu, Ikpo, Adedapo, & Olanrewaju, 2016; Keri, Hiremathad, Budagumpi & Nagaraja, 2015; Barot, Nikolova, Ivanov, & Ghate, 2013; Gaba & Mohan, 2016; Bansal & Silakari, 2012; Yadav & Ganguly, 2015). Besides the benzimidazole derivatives clinically used as antihypertensive agents mentioned above, benzimidazole derivatives have been approved for other clinical applications, for example, irtemazole (uricosuric agent); astemizole (antihistaminic);

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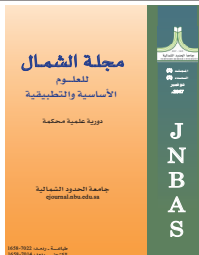
بحث مرجعي

مشتقات البينزيميدازول: دعامة مهمة لتطوير مضادات جديدة لمستقبلات الأنجيوتنسين

محمد عمران¹*، نيرة نعيم¹، سعيد الفقي¹، عبدالحكيم بوادقجي²

ملخص البحث: إن ارتفاع ضغط الدم هو أحد المسببات الرئيسية للوفاة بالعالم، وكذلك في المملكة العربية السعودية، كما أن انتشار هذا المرض في تزايد مستمر عند جميع الفئات العمرية في جميع أنحاء العالم، مما يحفز بضرورة القيام بالعديد من البحوث العلمية في هذا المجال. فقد وُجد أن نظام الرينين أنجيوتنسين هو المتسبب في ارتفاع مستوى ضغط الدم، وأن هذا النظام يمكن أن يتأثر بالعديد من الأدوية ومنها مثبطات الرينين، ومثبطات الإنزيمات المحولة للأنجيوتنسين، ومستقبلات الأنجيوتنسين2. وظهر حديثاً بعض المركبات الكيميائية من مشتقات البينزيميدازول التي يمكن أن تشكل داعماً أساسياً لتطوير مضادات مستقبلات الأنجيوتنسين2 لعلاج ضغط الدم. وبالمقابل فقد أجازت الهيئة الأمريكية للغذاء والدواء ثلاثة مركبات من مشتقات البينزيميدازول هي، كانديستران وتيلميسارتان وأزيلسارتان، بهدف علاج مرض ضغط الدم والأمراض المتعلقة بالقلب. واعتماداً على الدراسات السابقة وبيانات الأبحاث العلمية الحديثة التي تتناول مشتقات البينزيميدازول كمضادات لمستقبلات الأنجيوتنسين فقد تم بيان أثرها على علاج ضغط الدم والأمراض المتعلقة به مع التأكيد على الحفاظ عى فعاليتها ومدة استمراريتها وإتاحتها الحيوية. نُشرت أيضا العديد من البحوث التي توضح أهمية مشتقات البنزيميدازول في الكيمياء الطبية وفي تطوير هذه المركبات للاستخدام السريري. وسيتم في هذه الورقة العلمية تسليط الضوء على تطوير المشتقات الجديدة للبينزيميدازول كمضادات لمستقبلات الأنجيوتنسين التي لها المقدرة في المستقبل لتكون من الأدوية المعتمدة لعلاج ارتفاع ضغط الدم.

الكلمات المفتاحية: مشتقات البينزيميدازول؛ مضادات مستقبلات الأنجيوتنسين؛ ضغط الدم.

* للمراسلة:

(1)* قسـم الكيميــاء الصيدلية، كليــة الصيدلة جامعــة الحدود الشــمالية، ص.ب 840، رفحــاء 91911، المملكة العربية السـعودية.
e-mail: mohammed.baksh@nbu.edu.sa & imran_inderlok@yahoo.co.in

(2) عمادة البحث العلمي، جامعة الحدود الشمالية، ص.ب 1321، عرعر91431، المملكة العربية السعودية.

REVIEW ARTICLE

BENZIMIDAZOLE DERIVATIVES: AN IMPORTANT SCAFFOLD FOR THE DEVELOPMENT OF NEWER ANGIOTENSIN RECEPTOR ANTAGONISTS

Mohd. Imran[1]*, Naira Nayeem[1], Said A. El-Feky[1], Abdulhakim Bawadekji[2]

Abstract: Hypertension is a major cause of death worldwide as well as one of the main causes of death in Saudi Arabia. The prevalence of this disease is increasing in all age groups throughout the world which advocates that there is a need for more research in the field of hypertension. The renin angiotensin system (RAS) is implicated in the pathogenesis of hypertension. The renin inhibitors, angiotensin converting enzyme (ACE) inhibitors, and angiotensin II receptor (AT_1) antagonists are the drugs that affect renin angiotensin system to control hypertension. Recently, benzimidazole derivatives have emerged as an important scaffold for the development of angiotensin II, Type I (AT_1) receptor antagonists for the treatment of hypert. Three benzimidazole derivatives, namely, candesrtan, telmisartan, and azilsartan, have already been approved by the USFDA for the treatment of hypertension and related cardiac conditions. Based on the reported structure activity relationship studies and literature, newer benzimidazole derivatives as AT_1 receptor antagonists are being developed to tackle the issues related to hypertension and related cardiac conditions with emphasis to maintain their potency, duration of action, and bioavailability. Many reviews have been published that provide the importance of benzimidazole derivatives in medicinal chemistry and in the development of medicinal compounds for clinical use. However, this review highlights the development of newer benzimidazole derivatives as potential AT_1 receptor antagonists that may be able to see the light of future as approved drugs for the treatment of hypertension.

Keywords: Benzimidazole derivatives; Angiotensin receptor (AT_1) antagonists; Hypertension.

* Corresponding Author:
(1)* Department of Pharmaceutical Chemistry, Faculty of Pharmacy, Northern Border University, P.O. Box 840, Rafha 91911, Kingdom of Saudi Arabia.
e-mail: mohammed.baksh@nbu.edu.sa & imran_inderlok@yahoo.co.in
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compare results. Moreover, according to the SN ratio, dwell time was insignificant according to this confidence level (p-value of 0.084). This is true for a significance level of 95%, but if one considered a lower significance level "say 90%", then dwell time would be identified as a significant factor as well. However, this does not change the fact that the most significant factor was the tool rotational speed (highest F-vale) followed by the pin length. In summary, in terms of significance, the friction stir welding parameters can be divided into two sets. The first consists of the very significant factors of rotational speed and pin length while the second comprises the set of the least significant factors, shoulder width and dwell time.

CONCLUSION

Friction stir spot welding parameters for joining Al 6061 alloys were investigated in this work. There are four parameters that would affect the quality of the weld and hence the strength of the weld. These are tool rotational speed, pin length, dwell time and shoulder width. In order to accomplish a wide range of parameter possibilities, a Taguchi experimental design was implemented. The results of the study show that tool rotational speed was the most significant factor for determining the strength of the welded joints followed by pin length. Also, the study showed that dwell time was an insignificant factor in determining the strength of the welded joints. Finally, optimum parameter settings for FSSW Al6061 alloys within the factors investigated and their corresponding levels to achieve high strength welds are identified. These optimum parameters are as follows: tool rotational speed of 1120 rpm, pin length of 4.5 mm, shoulder width of 15 mm and dwell time 35 sec.

ACKNOWLEDGMENTS

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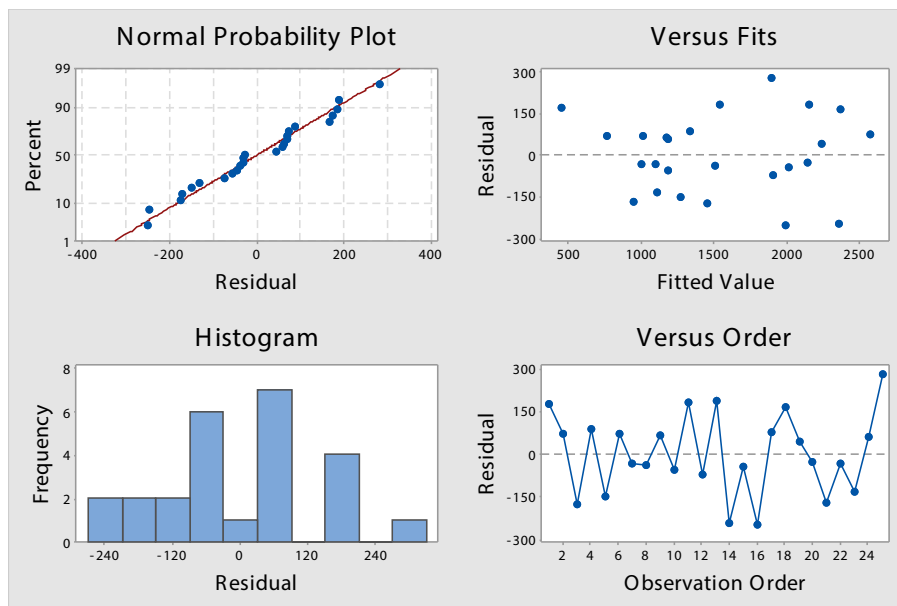Gerlich, Adrian, Yamamoto, Motomichi, North, Thomas

Figure 5: Residual plots for the mean of the force analysis of the data.

of a verification of the significance of the rotational speed and that it is the most significant factor. This result is most reasonable since friction stir welding in general is a solid-state joining mechanism that depend greatly on the heat generated by friction. This generated heat is expected to increase as the friction increases by means of increasing rotational speed. In other words, rotational speed and friction are obviously strongly associated and influence the welding tremendously. However, there seem to be an upper ceiling for the effectiveness of this relationship. As the rotational speed is increased beyond 1120 rpm, the strength of the weld fell significantly as shown earlier. This effect may be due to different possibilities. The first is that the heat generated by the friction welding was large enough to cause the metal to melt which causes severe structural modifications that did not exist in lower rotational speeds and hence hinder the quality of the weld causing it to withstand much less forces. The other possibility may be related to plasticity and solidification. The high rotational speed increases the plasticity of the material due to the generated heat and yet not allow it enough time to go through a proper solidification process thus not allowing the material to recrystallize and grow properly leading to low joint quality and poor strength.

Considering the insignificant factors in this study, the most insignificant factor was dwell time. This factor represents the amount of time that the tool spends within the joint after reaching the specified joint depth before being retracted. This factor is of special importance in the industry. Friction stir spot welds are used widely in automobile applications as a replacement to rivets and other joining methods. Automobile manufacturers for example join metal sheets and other parts together by different means of joining mechanisms on a daily basis. Money and time saving on these procedures dictates the least allowable processing time. In other words, if automobile manufacturers would depend on FSSW, the dwell time has to be reduced significantly. Of course this has to be achieved while maintaining high quality and strong welds. Thus, the effect of reduced dwell time on the strength and quality of the welds as well as the significance of related factors would be interesting to investigate.

In view of the confidence level used for the statistical analysis; the confidence level used in this experiment was 95% or α=0.05. This means that there is a 95% chance that the mean of the force will always be within the specified mean values (for all factors) if one was to repeat the experiment or do samples for every different combination and
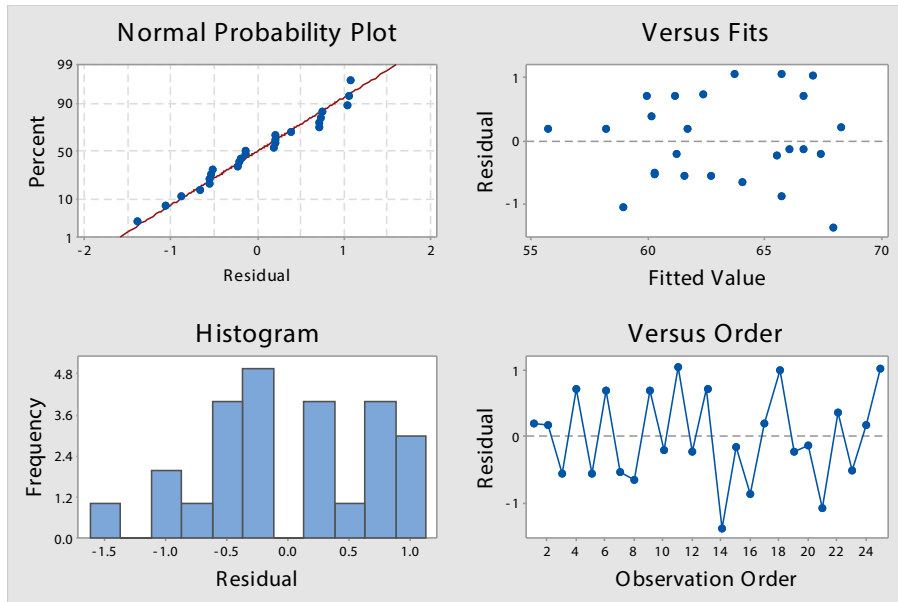
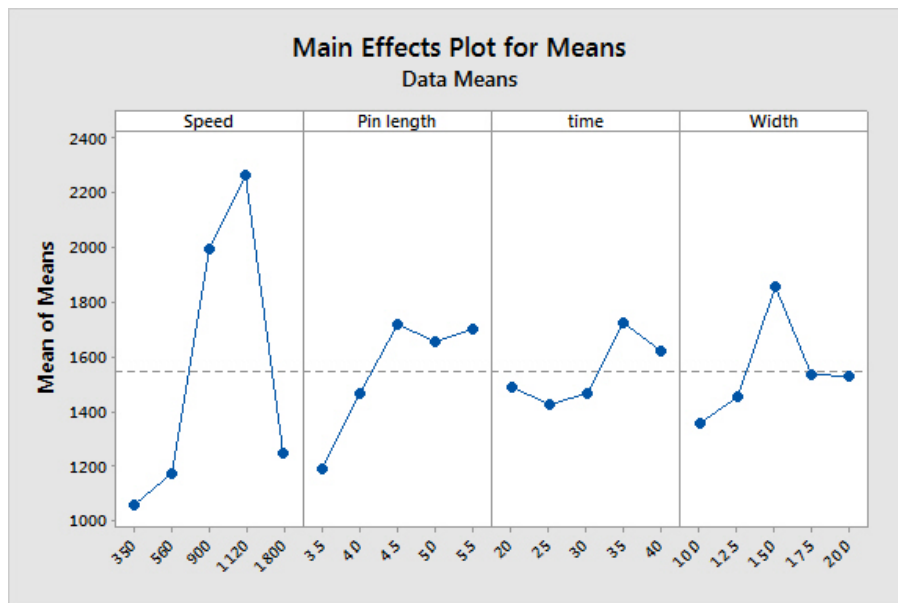**Figure 3: Residual plots for the SN ratio analysis of the data.**

Figure 4: Means of the force corresponding to all factors involved in the experiment.

4. DISCUSSION

It is clear from the ANOVA results that the most determining factor that increases the strength of welds produced by friction stir spot welding is the tool rotational speed. Also, the variation in the means of the force for this factor are higher than the remaining factors. For example, in the mean of the shear force analysis, the lowest mean value obtained was around 1050 kN for a rotational speed of 350 rpm while the largest mean was around 2200 kN for a rotational speed of 1120 rpm. The variations in the other factors were much less, mostly between 1200 and 1800 kN. This is an indication and sort

Table 3: the mean of the shear force according to the four variables and their corresponding levels (higher is better).

Level	Tool Speed	Pin length	Dwell time	Shoulder Width
1	1054	1188	1490	1354
2	1173	1467	1425	1451
3	1992	1716	1463	1856
4	2262	1655	1726	1534
5	1243	1699	1621	1530
Rank	1	2	4	3

same level as the SN ratio analysis and produced a force of 2262 kN), pin length of 4.5 mm (produced a force of 1716 kN), dwell time of 35 sec (the same level as the SN ratio analysis and produced a force of 1726 kN) and shoulder width of 15 mm (also the same level as the SN ratio analysis and produced a force of 1856 kN).

Table (3) the mean of the shear force according to the four variables and their corresponding levels (higher is better).

The corresponding statistical figures of the mean of the shear force analysis are discussed next. Figure (4) shows the means of the force vs all five levels

for all factors considered in this work. It is clear that the speed setting level 4 corresponding to tool rotational speed of 1120 rpm had the highest mean of shear force in the entire experiment and there were dramatic changes between the five levels of this factor. On the other hand, pin length results showed that pin lengths of 4.5 and 5.5 mm had almost the same mean with a slightly higher value for the 4.5 mm pin length. Although shoulder width and dwell time were not identified as a significant factors in the ANOVA of the mean of the shear force results, this figure shows that the shoulder width of 15 mm gave the highest mean compared to the other levels of this factor. In addition, dwell time of 35 sec gave the highest mean of shear force in the experiment for this factor.

Normal probability plot, histogram, residuals vs. fits and residuals vs. order of the mean of the force analysis are shown in Figure (5). The normal probability plot and the residuals vs. fits plot show acceptable normality of the data. Moreover, the residuals vs. order show good scatter around zero and hence indicating that the order by which the experiment was conducted is acceptable. On the other hand, the histogram plot of the mean of the force showed that the normality of the data was somehow acceptable.
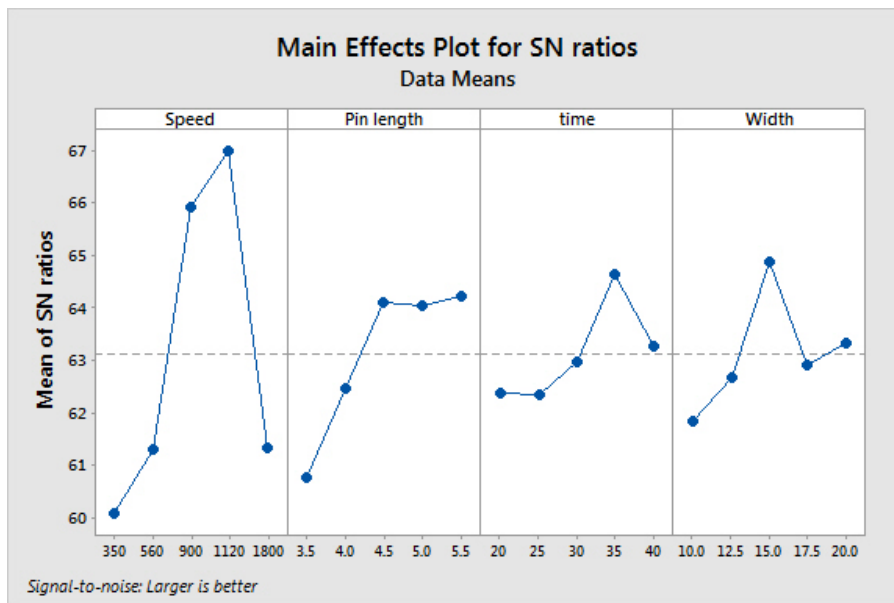

Figure 2: Means of the SN ratio for the entire experiment (larger is better).

3.1 Analysis of the SN Ratio of the Force

ANOVA results for the SN ratio of the force required to break the welded joints indicated the significance of the following factors: tool rotational speed, pin length and shoulder width; all with p-values < 0.05. Tool rotational speed had the highest significance with an F=34.19 and a corresponding p-value of 0.000. Pin length was the second significant factor with an F= 7.97 and a p-value of 0.007. Shoulder width had an F=4.46 and p-value of 0.035. According to the ANOVA results, dwell time was insignificant at this confidence level (p-value of 0.084).

On the other hand, the Response Table (RT) of the SN ratio showed some interesting results. The setting that was used for the SN ratio was "larger is better" since the preference is to achieve the highest possible shear force required to break the weld and hence the strongest possible weld. As a result, the RT indicated that the weld parameters combination for achieving the strongest weld in this case are: tool rotational speed of 1120 rpm, pin length of 5.5 mm, dwell time of 35 sec and shoulder diameter width of 15 mm, as shown in Table (2). The column showing "*Level*" is an indication of a specific welding parameter level. For example, tool rotational speed level 1 corresponds to 350 rpm and so on. Moreover, the rank at the bottom of the table ranks all welding parameters in terms of significance.

Table 2: SN ratio for the four variables and their corresponding levels (higher is better).

Level	Tool Speed	Pin length	Dwell time	Shoulder Width
1	60.08	60.78	62.39	61.84
2	61.30	62.47	62.36	62.67
3	65.94	64.12	62.98	64.88
4	67.00	64.07	64.64	62.92
5	61.33	64.22	63.28	63.34
Rank	1	2	4	3

The corresponding statistical figures of the SN ratio analysis are discussed next. Figure (2) shows the means of the SN ratios vs. all five levels for all factors considered in this work. It is clear that the

speed setting level 4 corresponding to tool rotational speed of 1120 rpm had the highest SN ratio in the entire experiment. In addition, pin length results show that pin lengths of 4.5, 5.0 and 5.5 mm had almost the same SN ratio with a slightly higher SN ratio for the 5.5 mm pin length. Although dwell time was not identified as a significant factor in the ANOVA results presented earlier, this figure shows that the dwell time of 35 sec gave the highest SN ratio compared to the other levels of this factor. Finally, the shoulder width showed that the best setting for achieving the largest SN ratio would be a shoulder width of 15 mm.

Normal probability plot, histogram, residuals vs. fits and residuals vs. order of the SN ratio analysis are shown in Figure (3). The normal probability plot and the residuals vs. fits plot show acceptable normality of the data. Moreover, the residuals vs. order show good scatter around zero and hence indicating that the order by which the experiment was conducted is acceptable. On the other hand, the histogram plot of the SN ratio showed that the data was slightly skewed.

3.2 Analysis of the Mean of the Shear Force

ANOVA results for the mean of the shear force showed that tool rotational speed and pin length were the only significant factors at alpha = 0.05 with p-values of 0.000 and 0.040 respectively. It also showed that the tool rotational speed was the most significant factor since it had the highest F-value (24.98) compared to 4.19 for the pin length. These results are similar to the SN ratio analysis presented in the last section in the sense that tool rotational speed was the most significant factor in the experiment. Also, the fact that dwell time was insignificant in both analyses. However, the mean of the shear force analysis differs in the fact that the shoulder width is not significant anymore.

On the other hand, the RT of the means of the shear force showed somehow similar results to those of the SN ratio response table presented and discussed earlier. The same setting "larger is better" was used here as well since we are interested in the largest possible force. According to Table (3), the parameter settings combination that should be used in order to achieve the strongest weld are as follows: tool rotational speed of 1120 rpm (the

Table 1: Details of TED.

| Exp. No.	Speed (rpm)	Pen length (mm)	Dwell time (sec)	Shoulder diameter (mm)	Exp. No.	Speed (rpm)	Pen length (mm)	Dwell time (sec)	Shoulder diameter (mm)
1	350	3.5	20	10	14	900	5	20	15
2	350	4	25	12.5	15	900	5.5	25	17.5
3	350	4.5	30	15	16	1120	3.5	35	12.5
4	350	5.0	35	17.5	17	1120	4	40	15
5	350	5.5	40	20	18	1120	4.5	20	17.5
6	560	3.5	25	15	19	1120	5	25	20
7	560	4	30	17.5	20	1120	5.5	30	10.0
8	560	4.5	35	20	21	1800	3.5	40	17.5
9	560	5	40	10	22	1800	4	20	20
10	560	5.5	20	12.5	23	1800	4.5	25	10
11	900	3.5	30	20	24	1800	5	30	12.5
12	900	4	35	10	25	1800	5.5	35	15
13	900	4.5	40	12.5					
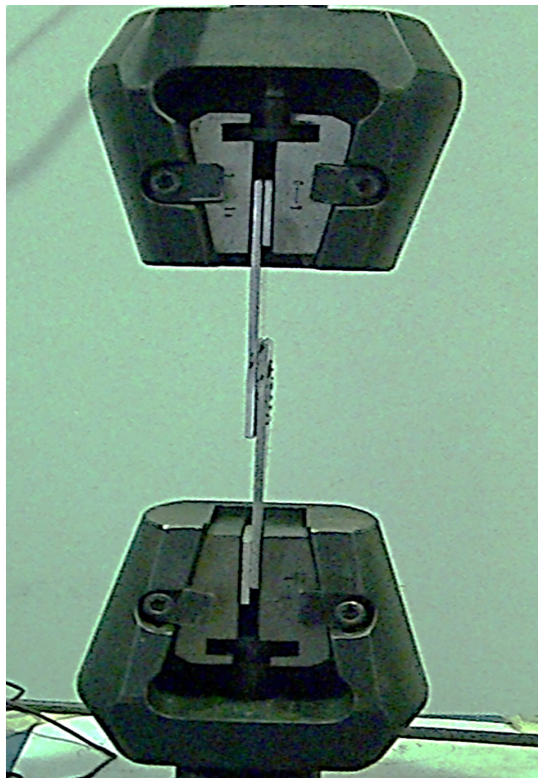
Figure 1: Lap shear test of one of the FSSW samples.

After conducting all 25 welds, the shear lap force required to break the welded joint was recorded for further statistical analysis. Further details about the actual experimental work and related information are published in Tashkandi *et al* (Tashkandi, Al-jarrah, & Ibrahim, 2017).

The force data along with TED were used to perform the analysis of variance (ANOVA) for the mean of the force to verify the significance of the test results, the significance of each variable, and any possible combinations. Moreover, ANOVA was performed for the signal to noise ratio (SN ratio) to obtain more robust statistical results. All statistical analyses were undertaken at a confidence level of 95%.

3. RESULTS

The results of the experiment are discussed in this section. There are two main parts to be discussed, the statistical analysis for the mean of the signal to noise (SN) ratio and the statistical analysis of the mean of the shear force. This section will represent ANOVA results for each part as well as corresponding figures and tables.

1. INTRODUCTION

Currently, a principal research objective of the machine industry is how to develop fast high quality welds that are both reliable and economical. Friction Stir Spot Welding (FSSW), a variant of Friction Stir Welding (FSW; TWI Abington, UK: 1995), has proven to be a most reliable source due to its superior fast quality welds and energy saving and cost cutting qualities (Baek, Choi, Lee, Ahn, Yeon, Song, & Jung, 2010; Jeon, Hong, Kwon, Cho, & Han, 2012; Yang, Fu, & Li, 2014). The research on FSSW has followed five different strands. The first relates to the microstructure and failure mechanisms of welding Al alloys (Babu, Sankar, Janaki Ram, Venkitakrishnan, Madhusudhan Reddy, & Prasad Rao, 2013; Mishra, 2007; Mitlin, Radmilovic, Pan, Chen, Feng, & Santella, 2006; Pathak, Bandyopadhyay, Sarangi, & Panda, 2013; Qiu, Iwamoto, & Satonaka, 2009); the second pertains to specific welding phenomena, such as local melting and tool slippage (Ahmad & Asmael, 2015; Gerlich, Avramovic-Cingara, & North, 2006; Gerlich, Su, & North, 2005; Gerlich, Adrian, Yamamoto, Motomichi, North, Thomas H, 2008); the third strand covers the mechanics of joining dissimilar materials, such as aluminum, magnesium and steel (Chen, Komazaki, Kim, Tsumura, & Nakata, 2008; Kulekci, 2014); the fourth area concerns the various welding parameters, specifically, how the parameters can be enhanced and/or optimized experimentally (Bilici, 2012; Bilici & Yükler, 2012; Yuan, Mishra, Webb, Chen, Carlson, Herling, & Grant, 2011) and, finally, the recent trend that has shifted toward friction stir spot welding using refill techniques whereby the key-hole left behind after the removal of welding tool is refilled with base material so as to increase the material's resistance to corrosion and related effects (Bakavos, Chen, Babout, & Prangnell, 2011; Paidar & Sarab, 2016; Xu, Li, Ji, & Zhang, 2017).

In this study, a Taguchi Experimental Design (TED) system that proved to be the most reliable tool to extrapolate the dimensions of the welding parameters of FSSW was used. First, as a statistical experiment design, TED enables the researcher to conduct the least number of experiments while yet providing a level of significance for process parameters and making a solid and sound conclusion about the optimum FSSW welding parameters for the type of material being considered. Second, given that FSSW has four main process parameters (tool rotational speed, plunge depth (aka pin length), dwell time, and shoulder width), if one were to undertake a comprehensive study of each these parameters, the amount of experiments, time, and costs, that would be required would be overwhelming. Third, studies that have investigated welding process parameters using alternative alloys, such as the 6060-T5 alloy, and/or other experimental design methods, have not yielded the results that the machine industry expects (Merzoug, Mazari, Berrahal, & Imad, 2010). Consequently, TED and Al6061 remain the most widely used design and alloy in the automotive industry, thus the objects of this study.

2. METHODOLGY

There are four FSSW weld parameters that are of interest to this study: tool rotational speed, shoulder diameter, plunge depth (pin length) and dwell time. In addition, there is one output of interest, which is the shear force that will break the weld. Each weld parameters had five levels to be tested. The tool rotational speed was varied from 350 to 1800 rpm. The Shoulder diameter was varied from 10 to 20 mm by 2.5 mm increments. The plunge depth was varied from 3 mm to 5 mm by 0.5 mm increments. Finally, the dwell time was varied from 20 to 40 seconds by 5 sec increments. Consequently, the design of the experiment required conducting 25 experiments to account for all variables and any possible significant combinations. As a result, 25 samples corresponding to the experimental design were produced for further force analysis. Table (1) shows details of the experiments that were designed using parameter variations corresponding to TED.

Aluminum 6061 alloys with a thickness of 3mm were used in this work. Two rectangular pates of 100*25mm were lap-welded by friction stir spot welding. A vertical conventional milling machine was used to produce the welds. A special fixture was fastened on the milling machine and was also used to tightly hold the samples in place to eliminate any vibrational effects. Friction stir spot welding was produced in each experiment according to the specified experimental design and the weld strength was then measured via a universal tensile testing machine as shown in Figure (1).

تحديد ودراسة العوامل المؤثرة في عملية اللحام بالاحتكاك الخلطي النقطي لسبائك الألمنيوم 6061 باستخدام تصميم التجارب

محمد بن عبدالعزيز طاشكندي[1]*

ملخص البحث: اللحام بالاحتكاك الخلطي النقطي هو من بين تقنيات اللحام المستخدمة على نطاق واسع وخاصة في صناعة السيارات. وكونه لحام في الحالة الصلبة للمادة، فإنه يعتمد على العديد من العوامل؛ أهم هذه العوامل هي سرعة دوران أداة اللحام، وطول دبوس اللحام، وعرض كتف أداة اللحام والوقت الساكن. تركز هذه الدراسة على دراسة مستويات مختلفة من هذه العوامل والحصول على مزيج من شأنه أن ينتج أقوى لحامات لسبائك الألمنيوم 6061 عبر اللحام بالاحتكاك الخلطي النقطي. تم استخدام أسلوب التحليل الإحصائي تاغوتشي لتقليل عدد التجارب المطلوبة لتغطية جميع العوامل والحصول على نتائج إحصائية ذات دلالة صحيحة. أشارت النتائج إلى أن أهم العوامل المؤثرة على قوة اللحام في سبائك الألمنيوم 6061 هي سرعة دوران أداة اللحام وطول دبوس اللحام.

الكلمات المفتاحية: اللحام بالاحتكاك الخلطي النقطي؛ عوامل اللحام بالاحتكاك الخلطي النقطي؛ تاغوتشي؛ قوة اللحام.

* للمراسلة:

(1)* قسـم الهندسـة الميكانيكية، كلية الهندسـة، جامعة الحدود الشـمالية، ص.ب 1321، عرعر 91431، المملكة العربية السـعودية.

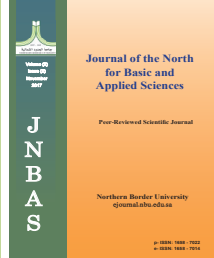e-mail: mtashkandi@nbu.edu.sa & tashkandi@gmail.com

IDENTIFYING AND STUDYING THE IMPACT OF SIGNIFICANT PROCESS PARAMETERS ON FRICTION STIR SPOT WELDING OF THE AL6061 ALLOY USING DOE

Mohammed A. Tashkandi [1*]

Abstract: Friction Stir Spot Welding (FSSW) is a solid-state multi-parameter welding process that is widely used especially in the automotive industry. This paper examines the manner in which its four primary parameters (tool rotational speed, pin length, shoulder width, and dwell time) can be employed to produce stronger welds for Al6061 alloys. A Taguchi Statistical Analysis system was utilized to minimize the number of experiments, costs, time and energy required for the parameters. Significant valid statistical results were obtained which suggested that tool rotational speed and pin length are the most significant factors for determining welded joints strength. Optimum parameter settings for FSSW Al6061 alloys within the factors were also investigated and the corresponding levels required to achieve high strength welds were identified.

* Corresponding Author:

(1)* Department of Mechanical Engineering, College of Engineering, Northern Border University, P.O. Box 1321, Arar 91431, Kingdom of Saudi Arabia

e-mail: mtashkandi@nbu.edu.sa & tashkandi@gmail.com

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Table 6: MLEs and Information criterion.

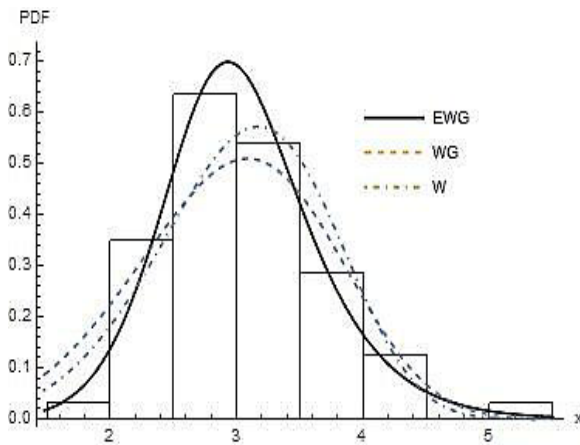| Model	Estimates				Information Criterion			
	a	β	y	p	-2log-likelihood	BIC	AIC	CAIC
EWG	0.00002035	8.07047	0.5678	0.8504	115.311	131.88	123.311	124.00066
WG	0.005356	4.4103	0	0.000106	125.983	138.41	131.983	132.3898
W	0.002355	5.04942	0	0	123.914	132.20	127.917	128.114

Figure 10: Histogram and fitted PDFs.

Moreover, Figure (10) shows that the EWG model gives the better fit for the data; therefore, the proposed distribution provides a close fit as compared to its special cases.

CONCLUSIONS

This research introduces an Extended Weibull Geometric model; it discusses the expansions of moments, factorial moments, cumulants and entropies. The authors derive the moment and MLEs of order statistics. Simulation outcomes suggest that the estimation performance is satisfied. A real data set is used for the new model; it is suggests that the proposed distribution is better than its sub models. Consequently, the authors look hope the proposed model performs better than its class due to the flexibility and greater applicability of its sub models.

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Table 3: Estimates, log-likelihood and *p*-values.

		n=100	*n*=200	*n*=300
Parameter Estimates	*α* = 2.12	2.29648 (8.07864)	1.69358 (149.795)	2.72556 (183.092)
	β = 4.8	6.70782 (0.533014)	5.49098 (1.33439)	5.11727 (1.13178)
	γ = 1.15	2.16503 (0.392509)	1.62326 (0.731233)	1.03546 (0.766765)
	p = 0.2	0.587932 (0.112324)	0.505057 (0.0505055)	0.000272122 (0.0983515)
Log-Likelihood		-15.495	-54.669	-56.1007
p-values	**Anderson Darling**	0.430452	0.756026	0.435584
	Kolmogorov-Smirnov	0.51079	0.485762	0.516989
	Pearson	0.663219	0.368969	0.264803

Table 4: Gauge lengths of 10mm.

1.901	2.132	2.203	2.228	2.257	2.350	2.361	2.396	2.397	2.445	2.454	2.474
2.518	2.522	2.525	2.532	2.575	2.614	2.616	2.618	2.624	2.659	2.675	2.738
2.740	2.856	2.917	2.928	2.937	2.937	2.977	2.996	3.030	3.125	3.139	3.145
3.220	3.223	3.235	3.243	3.264	3.272	3.294	3.332	3.346	3.377	3.408	3.435
3.493	3.501	3.537	3.554	3.562	3.628	3.852	3.871	3.886	3.971	4.024	4.027
4.225	4.395	5.020									

Table 5: Descriptive statistics.

Data	Mean	Median	S.D	Variance	Skewness	Kurtosis
Gauge lengths (10mm)	3.05930	2.99600	0.6209	0.386	0.648	0.412

This study takes criteria, such as the -2log-likelihood, the Bayesian Information Criteria (BIC), the Akaike Information Criteria (AIC) and the Consistent Akaike Information Criteria (CAIC). However, Table (6) shows that the EWG distribution provides the smallest values than the WG distribution and Weibull distribution for these statistics; therefore, our EWG distribution is better than its sub models. Figure (10) shows the histogram of the data and fitted EWG, WG and W.

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$$\frac{\partial L}{\partial \beta} = \frac{n}{\beta} + \sum_{i=1}^{n} \ln x_i - (\gamma+1)\alpha \sum_{i=1}^{n} \frac{x_i^{\beta} \ln(x_i)}{\left(1+\gamma\alpha x_i^{\beta}\right)} - 2p\alpha \sum_{i=1}^{n} \frac{x_i^{\beta} \ln(x_i)\left(1+\gamma\alpha x_i^{\beta}\right)^{-\left(1+\frac{1}{\gamma}\right)}}{\left[1-p\left(1+\gamma\alpha x_i^{\beta}\right)^{-1/\gamma}\right]} \qquad (36)$$

$$\frac{\partial L}{\partial \gamma} = \alpha \sum_{i=1}^{n} \frac{x_i^{\beta}}{\left(1+\gamma\alpha x_i^{\beta}\right)} - \frac{1}{\gamma^2} \sum_{i=1}^{n} \ln\left(1+\gamma\alpha x_i^{\beta}\right) + \frac{\alpha}{\gamma} \sum_{i=1}^{n} \frac{x_i^{\beta}}{\left(1+\gamma\alpha x_i^{\beta}\right)} + \frac{2p\alpha}{\gamma} \sum_{i=1}^{n} \frac{x_i^{\beta}\left(1+\gamma\alpha x_i^{\beta}\right)^{-\left(1+\frac{1}{\gamma}\right)}}{\left[1-p\left(1+\gamma\alpha x_i^{\beta}\right)^{-1/\gamma}\right]}$$

$$\hspace{15cm} (37)$$

$$\frac{\partial L}{\partial p} = \frac{n}{(1-p)} - 2\sum_{i=1}^{n} \frac{\left(1+\gamma\alpha x_i^{\beta}\right)^{-1/\gamma}}{\left[1-p\left(1+\gamma\alpha x_i^{\beta}\right)^{-1/\gamma}\right]}. \qquad (38)$$

The maximum likelihood estimates are obtained by putting these terms equal to zero and solving simultaneously.

The simulation consequences are given in Table (3).

5. SIMULATION OF EWG DISTRIBUTION

The study discusses the simulation of EWG distribution, the goodness of fit of the proposed model tells how well it fits with artificial observations. The measures used for this purpose include the Kolmogorov- Smirnov test, Pearson's chi-squared test, and the Anderson- darling test.

A Monte Carlo simulation study with sample size $n = 100$, 200 and 300, with 1000 replicates, are considered. Moreover, the study observes that the estimated value is quite close to the corresponding observed value as the sample size is large as shown in Figures (9a & 9b), and very clear in Figure (9c). The simulation consequences are given in Table (3).

6. APPLICATION OF EWG DISTRIBUTION

This section demonstrates the flexibility and applicability of the proposed distribution using a well-known data set. The proposed model is compared with the Weibull Geometric (WG) distribution and the Weibull (W) distribution. For illustrative purpose, the data set in Table (4) are gauge lengths of 10mm and the sample size for the data set is sixty three from Kundu and Gupta (2006). However, the descriptive statistics is presented as in Table (5).

Afify, Yousof, Cordeiro, Ortega & Nofal (2016) also used the Transmuted Weibull Lomax (TWL) distribution for this data.
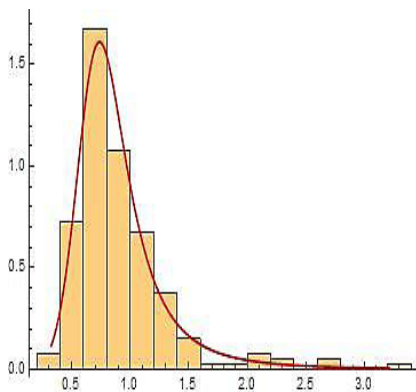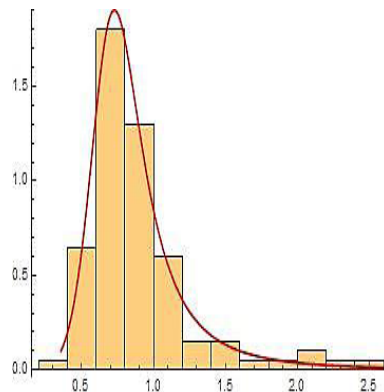

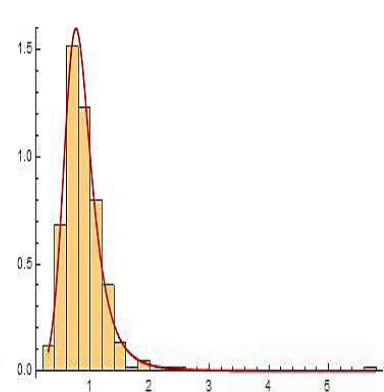
Figure 9a: Forn=100   Figure 9b: Forn=200   Figure 9c: Forn=300.

$$A(x) = \frac{(\alpha\beta)^{s-1}(1-p)^s}{\gamma(\gamma\alpha)^{(s-1)+\frac{1}{\beta}(1-s)}} \sum_{k=0}^{\infty} \binom{2s+k-1}{2s-1} p^k B\left(\frac{1}{\gamma}(s+k)+\frac{1}{\beta}(s-1), s+\frac{1}{\beta}(1-s)\right) \qquad (31)$$

$$H_R(f) = \frac{\log}{1-s}\left[\frac{(\alpha\beta)^{s-1}(1-p)^s}{\gamma(\gamma\alpha)^{(s-1)+\frac{1}{\beta}(1-s)}} \sum_{k=0}^{\infty} \binom{2s+k-1}{2s-1} p^k B\left(\frac{1}{\gamma}(s+k)+\frac{1}{\beta}(s-1), s+\frac{1}{\beta}(1-s)\right)\right]. \qquad (32)$$

where

$$s+\frac{1}{\beta} > \frac{s}{\beta}; \; s+\frac{1}{\beta} < \frac{s}{\beta} \quad s, \beta \quad \text{should not be integer anymore.}$$

$$\frac{1}{\gamma}(s+k)+\frac{s}{\beta} > \frac{1}{\beta}; \; \frac{1}{\gamma}(s+k)+\frac{s}{\beta} < \frac{1}{\beta} \quad s,k,\gamma,\beta \quad \text{should not be an integer anyone.}$$

The Beta entropy is given as

$$H_s(f) = \frac{1}{s-1}\left[1 - \int_0^{\infty} f^s(x)dx\right]$$

From Eq. (31) the Beta entropy of EWG distribution is given by

$$= \frac{1}{s-1}\left[1 - \frac{(\alpha\beta)^{s-1}(1-p)^s}{\gamma(\gamma\alpha)^{(s-1)+\frac{1}{\beta}(1-s)}} \sum_{k=0}^{\infty} \binom{2s+k-1}{2s-1} p^k B\left(\frac{1}{\gamma}(s+k)+\frac{1}{\beta}(s-1), s+\frac{1}{\beta}(1-s)\right)\right] \qquad (33)$$

4. MAXIMUM LIKELIHOOD ESTIMATION (MLEs) OF EWG DISTRIBUTION

The study presented, MLEs of the parameters α, β, γ and p. The random sample for size n like $\chi_1,.....,\chi_n$ from the EWG $(\alpha, \beta, \gamma, p)$ distribution.

Through using Eq. (4) the likelihood function is obtained as

$$L(\alpha,\beta,\gamma,p;x) = n\left[\ln(\alpha)+\ln(\beta)+\ln(1-p)\right]+(\beta-1)\sum_{i=1}^{n}\ln x_i - \left(1+\frac{1}{\gamma}\right)\sum_{i=1}^{n}\ln\left(1+\gamma\alpha x_i^{\beta}\right)$$

$$-2\sum_{i=1}^{n}\ln\left[1-p\left(1+\gamma\alpha x_i^{\beta}\right)^{-\frac{1}{\gamma}}\right] \qquad (34)$$

the study partially differentiates Eq. (34) get the parameter estimates as

$$\frac{\partial L}{\partial\alpha} = \frac{n}{\alpha} - (\gamma+1)\sum_{i=1}^{n}\frac{x_i^{\beta}}{\left(1+\gamma\alpha x_i^{\beta}\right)} - 2p\sum_{i=1}^{n}\frac{x_i^{\beta}\left(1+\gamma\alpha x_i^{\beta}\right)^{-\left(1+\frac{1}{\gamma}\right)}}{\left[1-p\left(1+\gamma\alpha x_i^{\beta}\right)^{-1/\gamma}\right]} \qquad (35)$$

3.9 Order Statistics of EWG Distribution

In this subsection, some closed forms are derived for the order statistics. Now for minimum and maximum order , the $f(x)_{(1)}$ and $f(x)_{(n)}$ are given in Eqs. (28 & 29).

$$f_{X_{(1)}}(x) = \frac{n\alpha\beta(1-p)^n x^{\beta-1}\left(1+\gamma\alpha x^\beta\right)^{-\frac{1}{\gamma}(\gamma+n)}}{\left[1-p\left(1+\gamma\alpha x^\beta\right)^{-\frac{1}{\gamma}}\right]^{n+1}} \tag{28}$$

$$f_{X_{(n)}}(x) = \frac{n\alpha\beta(1-p)x^{\beta-1}\left(1+\gamma\alpha x^\beta\right)^{-\left(1+\frac{1}{\gamma}\right)}\left[1-\left(1+\gamma\alpha x^\beta\right)^{-\frac{1}{\gamma}}\right]^{n-1}}{\left[1-p\left(1+\gamma\alpha x^\beta\right)^{-\frac{1}{\gamma}}\right]^{n+1}} \tag{29}$$

The order moments for EWG distribution is

$$E\left(x^r\right) = \frac{n!(1-p)(-1)^{r/\beta}}{(i-1)!(n-i)!(\gamma\alpha)^{r/\beta}}\sum_{j=0}^{n-i}(-1)^j\binom{n-i}{j}\sum_{k=0}^{\infty}\binom{j+i+k}{j+i}(p)^k\sum_{l=0}^{r/\beta}(-1)^l\binom{r/\beta}{l}B\left(k-\gamma l+1, j+i\right) \tag{30}$$

where

$(k+1) > \gamma l,\ (k+1) < \gamma l;\ \ \text{k},\ \gamma,\ l$ should not be an integer anymore.

3.10 Measures of Uncertainty

The entropy is a measure of uncertainty. The larger the entropy, the larger the uncertainty in the data. As information function is the measure of the amount of information, then entropy is the average of the amount of information. In a communication system, the higher value of entropy describes the low information. Statistical entropy has a different interpretation; the higher entropy of the data shows that there is high randomness in the data.

3.10.1 Rényie entropy and Beta entropy

The Rényie entropy of EWG distribution is described as

$$H_R(f) = \frac{\log}{1-s}\left[\int_0^\infty f^s(x)dx\right] \text{Where } s \neq 1 \text{ and } s > 0$$

consider

$$A(x) = \int_0^\infty f^s(x)dx$$

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Suppose the random variable 'X' has an extended Weibull-geometric distribution X~ EWG (α, β, γ, p), then its reversed residual function is described as

$$m_n(t) = \frac{\sum_{i=0}^{n}\binom{n}{i}(-1)^i(t)^i(1-p)}{\gamma(\alpha\gamma)^{n-i/\beta}\sum_{j=0}^{2}\binom{2}{j}(p)^j(-1)^j}\left(1 - \frac{(\gamma\alpha t^\beta)^b}{(1+\gamma\alpha t^\beta)^b B(a,b)}\sum_{i=0}^{a-1}(-1)^i\binom{a-1}{i}\frac{(\gamma\alpha t^\beta)^i}{(1+\gamma\alpha t^\beta)^i(b+i)}\right)$$

(25)

where

$$a = -\frac{1}{\gamma}(j+1) - \left(\frac{n-i}{\beta}\right), b = \left(\frac{n-i}{\beta}\right)+1; \quad -\frac{1}{\gamma}(j+1) - \left(\frac{n-i}{\beta}\right) > 0 \text{ hold for all values}$$

$$(j+1) > \frac{\gamma(i-n)}{\beta}; \quad j, i, \gamma, \beta \quad \text{should not be an integer anymore.}$$

The moments of residual life are:

$$m'_n(t) = \frac{\sum_{i=0}^{n}\binom{n}{i}(-1)^i(t)^i(1-p)}{\left(1 - \frac{1-(1+\gamma\alpha t^\beta)^{-1/\gamma}}{1-p(1+\gamma\alpha t^\beta)^{-1/\gamma}}\right)\gamma(\alpha\gamma)^{n-i/\beta}\sum_{j=0}^{2}\binom{2}{j}(p)^j(-1)^j}\left(1 - \frac{(\gamma\alpha t^\beta)^b}{(1+\gamma\alpha t^\beta)^b B(a,b)}\sum_{i=0}^{a-1}(-1)^i\binom{a-1}{i}\frac{(\gamma\alpha t^\beta)^i}{(1+\gamma\alpha t^\beta)^i(b+i)}\right)$$

(26)

3.8 Probability Weighted Moments

The PWM of X is given as

$$\rho_{s,r} = E\left[(x^s)[F(x)]^r\right] = \int_0^\infty x^s [F(x)]^r f(x)dx$$

The Probability Weighted Moments (PWMs) of the EWG distribution is

$$\rho_{s,r} = \frac{(1-p)}{(\alpha\gamma)^{s/\beta}}\sum_{k=0}^{\infty}(r+k+1)(p)^k\sum_{i=0}^{s/\beta}(-1)^{i+\frac{s}{\beta}}\binom{s/\beta}{i}B(k-\gamma i+1, r+1)$$

(27)

where

$$(k+1) > \gamma i; \quad (k+1) < \gamma i, \quad k, \gamma, i \quad \text{should not be an integer anymore.}$$

$$\delta_1(X) = E(|X - \mu_1'|) = 2\mu_1'F(\mu_1') - 2t_1(\mu_1') \text{ and } \delta_2(X) = E(|X - m|) = \mu_1' - 2t_1(m) \text{ where } t_1(.)$$

is truncated moment of Eq. (19) and $\boldsymbol{F}(.)$ is distribution funtion in Eq. (5). The mean deviation about mean and median are

$$\delta_1(X) = \left\{ \begin{array}{c} \dfrac{2(1-p)\sum\limits_{k=0}^{\infty}(k+1)p^k}{(\gamma\alpha)^{1/\beta}\gamma} B\left(\dfrac{1}{\gamma}(k+1) - \dfrac{1}{\beta}, \dfrac{1}{\beta}+1\right)\left(\dfrac{1-(1+Y)^{-1/\gamma}}{1-p(1+Y)^{-1/\gamma}}\right) \\[4mm] -\dfrac{2(1-p)\sum\limits_{k=0}^{\infty}(k+1)p^k\left\{B(a_1,b_1) - \left[1 - \dfrac{(Y)^{b_1}}{(1+Y)^{b_1}B(a_1,b_1)}(Z)\right]\right\}}{\gamma(\alpha\gamma)^{1/\beta}\left(\dfrac{1-(1+Y)^{-\frac{1}{\gamma}}}{1-p(1+Y)^{-\frac{1}{\gamma}}}\right)} \end{array} \right\}. \tag{23}$$

where

$$Y = \gamma\alpha\mu_1'^{\beta}; Z = \sum_{i=0}^{a_1-1}(-1)^i\binom{a_1-1}{i}\frac{(Y)^i}{(1+Y)^i(b_1+i)}$$

and

$$\delta_2(X) = \left\{ \begin{array}{c} \dfrac{2(1-p)\sum\limits_{k=0}^{\infty}(k+1)p^k}{(\gamma\alpha)^{1/\beta}\gamma} B\left(\dfrac{1}{\gamma}(k+1) - \dfrac{1}{\beta}, \dfrac{1}{\beta}+1\right) \\[4mm] -\dfrac{2(1-p)\sum\limits_{k=0}^{\infty}(k+1)p^k\left\{B(a_1,b_1) - \left[1 - \dfrac{(V)^{b_1}}{(1+V)^{b_1}B(a_1,b_1)}(L)\right]\right\}}{\gamma(\alpha\gamma)^{1/\beta}\left(\dfrac{1-(1+V)^{-\frac{1}{\gamma}}}{1-p(1+V)^{-\frac{1}{\gamma}}}\right)} \end{array} \right\}. \tag{24}$$

where

$$V = \gamma\alpha m^{\beta}; L = \sum_{i=0}^{a_1-1}(-1)^i\binom{a_1-1}{i}\frac{(V)^i}{(1+V)^i(b_1+i)}.$$

3.7 Reversed Residual of EWG Distribution

The reversed residual:

$$m_n(t) = \int_t^{\infty}(x-t)^n f(x)dx$$

3.4 Quantile of EWG Distribution

The quantile of the Extended Weibull Geometric Distribution is defined from Eq. (5), which this study presents

$$x = \left[\frac{\left(\frac{a-1}{ap-1} \right)^{-\gamma} - 1}{\alpha \gamma} \right]^{1/\beta} \tag{20}$$

by putting in Eq. (20) can get median of x, where 'a' is uniformly distributed.

$$x = \left[\frac{\left(\frac{0.5}{1-(0.5)p} \right)^{-\gamma} - 1}{\alpha \gamma} \right]^{1/\beta} \tag{21}$$

3.5 Mode of EWG Distribution

This subsection tries to derive the mode of EW $(\alpha, \beta, \gamma, p)$ G distribution by taking the natural log of Eq. (4) and taking the derivation with respect to x

$$\frac{\beta - 1}{x} - \frac{(\gamma+1)\alpha\beta x^{\beta-1}}{1+\gamma\alpha x^{\beta}} - \frac{2\alpha\beta p x^{\beta-1}\left(1+\gamma\alpha x^{\beta}\right)^{-\left(1+\frac{1}{\gamma}\right)}}{\left[1-p\left(1+\gamma\alpha x^{\beta}\right)^{\frac{1}{\gamma}}\right]} = 0 \tag{22}$$

since it appears, the Eq. (22) does not have an implicit solution in the general case. Consequently, this study discusses numerically as in (Table 2); therefore, for various values of the parameters $\alpha, \beta, \gamma,$ and p the mode is given in Table (2).

When increasing α but β, γ and p constant then mode is decreasing. When β increases then the mode is also increases and the remaining parameters are constant. If γ increased and the other parameters are constant, then the mode is decreased. After some time, γ increasing but the values of the mode converge. However, when increases and α, β, γ are constant, then the mode is decreased.

Table 2: Mode of the EWGD.

$\alpha = 1$			$p = 0.1$			
β \ γ	1	2	3	4	5	6
2	0.55	0.48	0.43	0.40	0.37	0.34
3	0.77	0.71	0.67	0.64	0.62	0.59
4	0.86	0.82	0.79	0.77	0.75	0.73
5	0.90	0.88	0.85	0.84	0.82	0.80
6	0.93	0.91	0.89	0.88	0.86	0.85

3.6 Mean Deviations of EWG Distribution

The mean deviation of mean and median is expressed as

3.2 Incomplete Moments of EWG Distribution

The incomplete moments:

$$m_r = \int_0^x x^r f(x)\,dx$$

The incomplete moments denoted by m_r is described as

$$m_r = \frac{(1-p)}{\gamma(\alpha\gamma)^{r/\beta}} \sum_{k=0}^{\infty} (k+1)\, p^k (-1)^{\frac{r}{\beta}+1} \left(\frac{\left(1-\left(1+\gamma\alpha x^\beta\right)\right)^b}{B(a,b)} \sum_{i=0}^{a-1} (-1)^i \binom{a-1}{i} \frac{\left(1-\left(1+\gamma\alpha x^\beta\right)\right)^i}{b+i} \right) \tag{18}$$

where

$$a = 1 - \frac{1}{\gamma}(k+\gamma+1); b = \frac{r}{\beta}+1 \quad \text{and} \quad \gamma > (k+\gamma+1); \gamma < (k+\gamma+1)\ k, \gamma \qquad \text{should not be an integer}$$

anymore.

3.3 Truncated Moments of EWG Distribution

The truncated moments of the Extended Weibull Geometric Distribution is expressed as

$$t_r(x) = P\left(x^r / t_1 < x < t_2\right) = \frac{\int_{t_1}^{t_2} x^r f(x)\,dx}{F(t_2) - F(t_1)}$$

$$t_r(x) = \frac{(1-p)\sum_{k=0}^{\infty}(k+1)p^k \left\{ \begin{array}{c} B(a_r,b_r) - \left[1 - \frac{\left(\gamma\alpha t_2^\beta\right)^{b_r}}{\left(1+\gamma\alpha t_2^\beta\right)^{b_r} B(a_r,b_r)} \sum_{i=0}^{a_r-1}(-1)^i \binom{a_r-1}{i} \frac{\left(\gamma\alpha t_2^\beta\right)^i}{\left(1+\gamma\alpha t_2^\beta\right)^i (b_r+i)} \right] - \\[2ex] \left[\frac{\left(\gamma\alpha t_1^\beta\right)^{b_r}}{\left(1+\gamma\alpha t_1^\beta\right)^{b_r} B(a_r,b_r)} \sum_{j=0}^{a_r-1}(-1)^j \binom{a_r-1}{j} \frac{\left(\gamma\alpha t_1^\beta\right)^j}{\left(1+\gamma\alpha t_1^\beta\right)^j (b_r+j)} \right] \end{array} \right\}}{\gamma(\alpha\gamma)^{r/\beta} \left\{ \left[\frac{1-\left(1+\gamma\alpha t_2^\beta\right)^{-\frac{1}{\gamma}}}{1-p\left(1+\gamma\alpha t_2^\beta\right)^{-\frac{1}{\gamma}}} \right] - \left[\frac{1-\left(1+\gamma\alpha t_1^\beta\right)^{-\frac{1}{\gamma}}}{1-p\left(1+\gamma\alpha t_1^\beta\right)^{-\frac{1}{\gamma}}} \right] \right\}} \tag{19}$$

where

$$a_r = \frac{1}{\gamma}(k+1) - \frac{r}{\beta}; b_r = \frac{r}{\beta}+1 \quad \text{and} \quad (k+1) > \frac{r\gamma}{\beta}; (k+1) < \frac{r\gamma}{\beta}; r, \gamma, \beta, k \qquad \text{should not be an integer}$$

anymore.

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and

$$K_r = \frac{(1-p)}{\gamma(\gamma\alpha)^{r/\beta}}\left\{\left[\sum_{k=0}^{\infty}(k+1)p^k B(C_r,D_r)\right] - \sum_{j=1}^{r-1}\binom{r-1}{j-1}k_j\left[\sum_{k=0}^{\infty}(k+1)p^k\gamma^{j/\beta}B(C_{r-j},D_{r-j})\right]\right\} \quad (15)$$

The coefficient of skewnessis

$$\sqrt{\beta_1} = \frac{\sum_{j=0}^{3}\binom{3}{j}(-1)^j\frac{(1-p)^{j+1}}{\gamma^{j+1}(\gamma\alpha)^{3/\beta}}\left(\sum_{k=0}^{\infty}(k+1)p^k B(C_1,D_1)\right)^j\left(\sum_{k=0}^{\infty}(k+1)p^k B(C_{3-j},D_{3-j})\right)}{\left[\sum_{j=0}^{2}\binom{2}{j}(-1)^j\frac{(1-p)^{j+1}}{\gamma^{j+1}(\gamma\alpha)^{2/\beta}}\left(\sum_{k=0}^{\infty}(k+1)p^k B(C_1,D_1)\right)^j\left(\sum_{k=0}^{\infty}(k+1)p^k B(C_{2-j},D_{2-j})\right)\right]^{3/2}} \quad (16)$$

The coefficient of kurtosis is

$$\beta_2 = \frac{\sum_{j=0}^{4}\binom{4}{j}(-1)^j\frac{(1-p)^{j+1}}{\gamma^{j+1}(\gamma\alpha)^{4/\beta}}\left(\sum_{k=0}^{\infty}(k+1)p^k B(C_1,D_1)\right)^j\left(\sum_{k=0}^{\infty}(k+1)p^k B(C_{4-j},D_{4-j})\right)}{\left[\sum_{j=0}^{2}\binom{2}{j}(-1)^j\frac{(1-p)^{j+1}}{\gamma^{j+1}(\gamma\alpha)^{2/\beta}}\left(\sum_{k=0}^{\infty}(k+1)p^k B(C_1,D_1)\right)^j\left(\sum_{k=0}^{\infty}(k+1)p^k B(C_{2-j},D_{2-j})\right)\right]^{2}} \quad (17)$$

Figure (8a) presents change β while α, γ, p are fixed at 5, 0.15, 0.6 correspondingly. The β_1 and β_2 -3 cut x-axis for β =7. Therefore, when α = 5, β = 7, γ = 0.15 and p = 0.6, the EWG model becomes symmetrical. Also, Figure (8b) shows that for α = 5, β = 5.9, p = 0.5, and selected value for γ . Thus when α = 5,β = 5.9,γ = 0.2 and p = 0.5, the EWG model becomes symmetrical. In Figure (8c) β_1 and β_2 -3 cut x-axis on α = 5, β = 6.9, γ = 0.15 and p = 0.6 the EWG distribution is symmetrical.
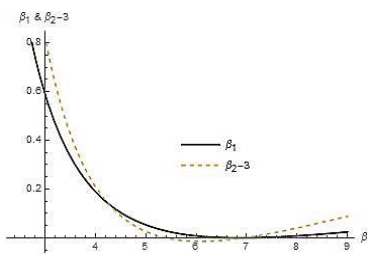

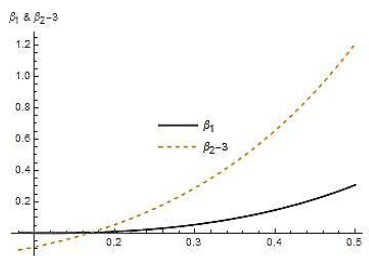**Figure 8a:** For α = 5, γ = 0.15, p = 0.6

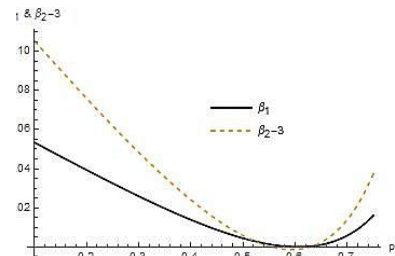**Figure 8b:** For α = 5, β = 5.9, p = 0.5

Figure 8c: For α = 5, β = 6.9, γ = 0.15

The mean and variance of EWG distribution is

$$\mu_1' = \frac{(1-p)}{\gamma(\gamma\alpha)^{1/\beta}} \sum_{k=0}^{\infty} (k+1) p^k B\left(\frac{1}{\gamma}(k+1) - \frac{1}{\beta}, \frac{1}{\beta} + 1\right) \tag{9}$$

$$Var(X) = \frac{(1-p)}{\gamma(\gamma\alpha)^{2/\beta}} \left\{ \left[\sum_{k=0}^{\infty} (k+1) p^k B\left(\frac{1}{\gamma}(k+1) - \frac{2}{\beta}, \frac{2}{\beta} + 1\right) \right] - \frac{(1-p)}{\gamma} \left[\sum_{k=0}^{\infty} (k+1) p^k B\left(\frac{1}{\gamma}(k+1) - \frac{1}{\beta}, \frac{1}{\beta} + 1\right) \right]^2 \right\} \tag{10}$$

The negative moments are

$$\mu_{-r}' = E(X^{-r}) = \frac{(1-p)}{\gamma(\gamma\alpha)^{-\frac{r}{\beta}}} \sum_{k=0}^{\infty} (k+1) p^k B\left(\frac{r}{\beta} + \frac{1}{\gamma}(k+1), 1 - \frac{r}{\beta}\right) \tag{11}$$

where $1 > \frac{r}{\beta}$; $1 < \frac{r}{\beta}$ r, β should not be an integer anyone.

The fractional moments are

$$E\left(X^{1/r}\right) = \frac{(1-p)}{\gamma(\gamma\alpha)^{1/\beta r}} \sum_{k=0}^{\infty} (k+1) p^k B\left(\frac{1}{\gamma}(k+1) - \frac{1}{\beta r}, \frac{1}{\beta r} + 1\right) \tag{12}$$

where $(k+1) > \frac{\gamma}{\beta r}$; $(k+1) < \frac{\gamma}{\beta r}$ k, γ, β, r should not be an integer anyone.

The pth descending factorial moment for EWG distribution is

$$\mu_{(p)}' = E\left[X^{(p)}\right] = E\left[X(X-1) \times \ldots \times (X-p+1)\right] = \sum_{m=0}^{p} s(p,m) \mu_m'$$

where
$$s(p,m) = (m!)^{-1} \left[\frac{d^m}{dx^m} x^{(p)}\right]_{x=0}$$

is the Striling number of the first kind, and where one can obtain the factorial moments by using the expression of Eq. (8)

$$\mu_{(p)}' = \sum_{m=0}^{p} s(p,m) \frac{(1-p)}{\gamma(\gamma\alpha)^{m/\beta}} \sum_{k=0}^{\infty} (k+1) p^k B\left(\frac{1}{\gamma}(k+1) - \frac{m}{\beta}, \frac{m}{\beta} + 1\right). \tag{13}$$

The central moments and cumulants are

$$\mu_r = \sum_{j=0}^{r} \binom{r}{j} (-1)^j \frac{(1-p)^{j+1}}{\gamma^{j+1}(\gamma\alpha)^{r/\beta}} \left[\sum_{k=0}^{\infty} (k+1) p^k B(C_1, D_1)\right]^j \left[\sum_{k=0}^{\infty} (k+1) p^k B(C_{r-j}, D_{r-j})\right] \tag{14}$$

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Table (1) is presented Sub models of EWG distribution for the parameters α, β, γ and p with its crossbonding *f*(x).

3. PROPERTIES

This section derives statistical expressions for EWG distribution such as moments, quantile, mode and entropies, etc.

Table 1: Sub models of EWG distribution.

Model	α	β	γ	p	f(x)
WG	α	β	$\gamma \to 0$	p	$f(x) = \dfrac{\alpha\beta(1-p)x^{\beta-1}e^{-\alpha x^{\beta}}}{\left(1-pe^{-\alpha x^{\beta}}\right)^{2}}$
EW	α	β	γ	0	$f(x) = \alpha\beta x^{\beta-1}\left(1+\gamma\alpha x^{\beta}\right)^{-\frac{1}{\gamma}-1}$
Weibull	α	β	$\gamma \to 0$	0	$f(x) = \alpha\beta x^{\beta-1}e^{-\alpha x^{\beta}}$
EE	α	1	γ	0	$f(x) = \alpha\left(1+\gamma\alpha x\right)^{-\frac{1}{\gamma}-1}$
Exponential	α	1	$\gamma \to 0$	0	$f(x) = \alpha e^{-\alpha x}$
Rayleigh	α	2	$\gamma \to 0$	0	$f(x) = 2x\alpha e^{-\alpha x^{2}}$
Extended Rayleigh	α	2	γ	0	$f(x) = 2x\alpha\left(1+\gamma\alpha x^{2}\right)^{-\frac{1}{\gamma}-1}$
LL	1	β	1	0	$f(x) = \dfrac{\beta x^{\beta-1}}{\left(1+x^{\beta}\right)^{2}};$

3.1 The Moments of EWG Distribution

The moment of EWG distribution is described as

$$\mu'_r = \frac{(1-p)}{\gamma(\gamma\alpha)^{r/\beta}} \sum_{k=0}^{\infty}(k+1)p^k B\left(C_r, D_r\right) \qquad (8)$$

where
$C_r = \dfrac{1}{\gamma}(k+1) - \dfrac{r}{\beta}, \; D_r = \dfrac{r}{\beta} + 1; \; (k+1) > \dfrac{r\gamma}{\beta}, \; (k+1) < \dfrac{r\gamma}{\beta} \; r, \gamma, \beta, k$ should not be an integer anymore.

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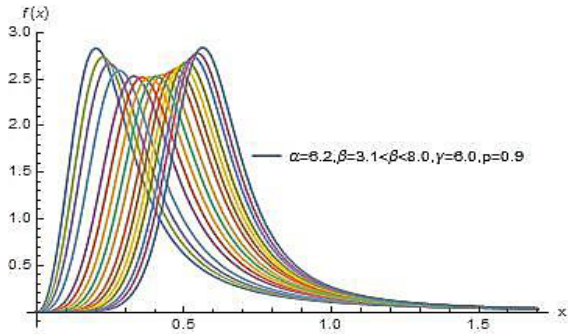
Figure 2: β effects while fixing α, γ and p
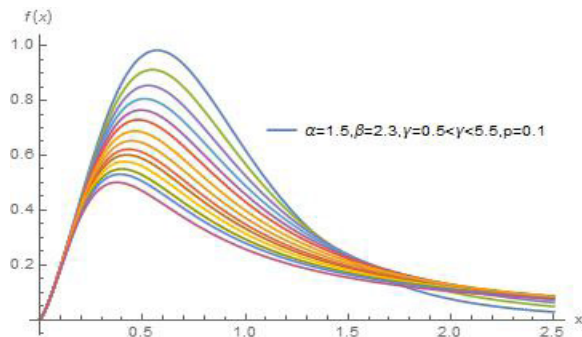
Figure 3: γ effects while fixing α, β and p.
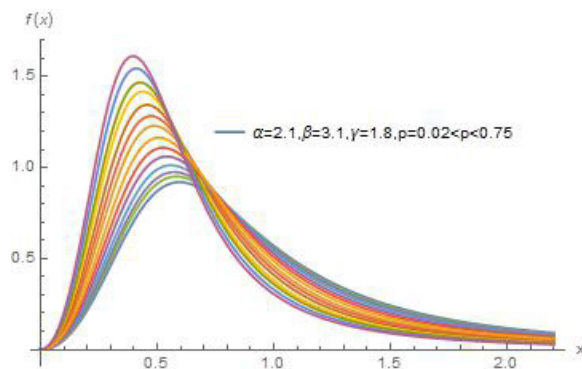
Figure 4: p effects while fixing α, β and γ.

The Cumulative Distribution Function (CDF) of the Exponentiated Weibull-Geometric (EWG) distribution is given as

$$F(x) = \frac{1 - \left(1 + \gamma\alpha x^{\beta}\right)^{-\frac{1}{\gamma}}}{1 - p\left(1 + \gamma\alpha x^{\beta}\right)^{-\frac{1}{\gamma}}};$$

$$x > 0, \alpha > 0, \beta > 0, \gamma > 0, p \in (0,1) \tag{5}$$

The survival and hazard functions of the EWG distribution are given as;

$$S(x) = \frac{\left(1 + \gamma\alpha x^{\beta}\right)^{-\frac{1}{\gamma}}(1 - p)}{1 - p\left(1 + \gamma\alpha x^{\beta}\right)^{-\frac{1}{\gamma}}} \tag{6}$$

$$h(x) = \frac{\alpha\beta x^{\beta-1}}{\left(1 + \gamma\alpha x^{\beta}\right)\left[1 - p\left(1 + \gamma\alpha x^{\beta}\right)^{-\frac{1}{\gamma}}\right]} \tag{7}$$

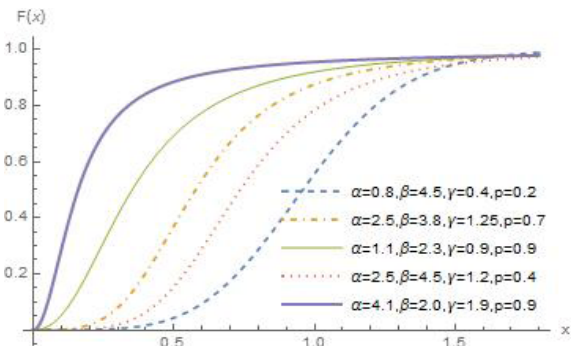The $F(x)$, $S(x)$ and $h(x)$ with its graph is given as shown in Figures (5, 6, and 7) respectively.
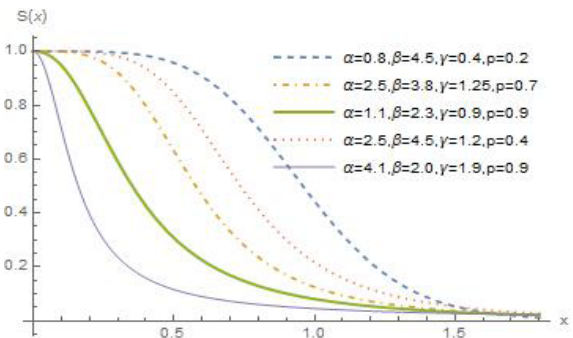

Figure 5: The graph of CDF.

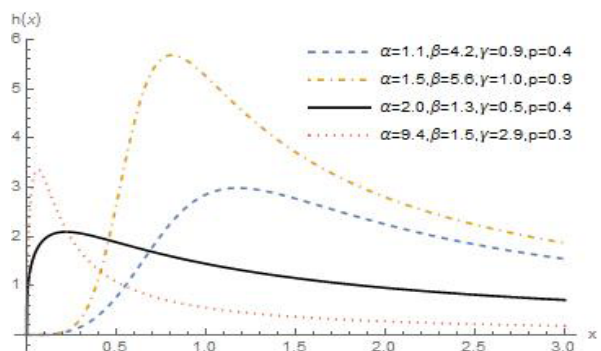**Figure 6: The graph of the survival function.**

Figure7: The graph of the hazard function.

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1. INTRODUCTION

The Weibull Distribution was introduced by the Swedish physicist Waloddi Weibull (Weibull, 1939) to explain the behavior of the breaking strength of materials. In statistics, there are many lifetime distributions but the Weibull Distribution is much flexible in potential as compared to other lifetime distributions. This distribution gives increasing, decreasing and constant hazard rates. Several researchers have proposed different forms of the Weibull Distribution to attain non-monotonic shapes, such as bathtub shapes. The Weibull Distribution has been used in different fields; some examples are discussed, such as, Inverse Weibull model analyzed reliability analysis for commercial vehicle engines (Keller, Giblin, & Farnworth, 1985). Further studied used the Exponentiated Weibull Distribution with some application for bus-motor failure data and flood data (Mudholkar, Srivastava & Freimer, 1995; Mudholkar and Hutson, 1996).

By combining the well-known distributions one can get new distribution with more parameters which generally have a flexible failure rate with applications to data modeling. Adamidis and Loukas (1998) discussed the Exponential Geometric Distribution. They developed several interesting properties and its hazard rate function is decreasing. Kuş (2007) explained the Exponential Poisson Two Parameter Distribution which accommodates decreasing hazard rates. Barreto-Souza *et al* examined the Weibull-Geometric Distribution (WG) and studied its different properties (Barreto-Souza, de Morais & Cordeiro, 2011). The WG distribution contains special sub-models such as extended exponential geometric distribution, the exponential geometric distribution and Weibull distribution. Wang and Elbatal (2015) proposed the Modified Weibull Geometric Distribution. It is discussed through compounding the Modified Weibull with the geometric distributions.

2. THE NEW DISTRIBUTION

Let z be a discrete random variable with the following probability mass function:

$$f(z) = (1-p)p^{z-1} \tag{1}$$

where $\quad z = 1, 2, 3, \ldots$ and $0 < p < 1$.

(Hashimoto, Ortega, Cordeiro & Pascoa, 2015) defined probability density and cumulative density function for the Extended Weibull (EW) model as:

$$f(x) = \alpha\beta x^{\beta-1}\left(1+\gamma\alpha x^{\beta}\right)^{-\frac{1}{\gamma}-1}; \; x > 0 \tag{2}$$

$$F(x) = 1-\left(1+\gamma\alpha x^{\beta}\right)^{-\frac{1}{\gamma}}; \; x > 0 \tag{3}$$

For indicates scale; $\gamma > 0$, $\beta > 0$ indicate shapes parameters.

The Extended Weibull Geometric Distribution is defined as

$$f(x) = \frac{\alpha\beta(1-p)x^{\beta-1}\left(1+\gamma\alpha x^{\beta}\right)^{-\left(1+\frac{1}{\gamma}\right)}}{\left(1-p\left(1+\gamma\alpha x^{\beta}\right)^{-\frac{1}{\gamma}}\right)^{2}}; \; x > 0 \tag{4}$$

where $\alpha > 0, \beta > 0, \gamma > 0$ and $p \in (0,1)$; α is scale β, γ are shape parameters.

Figure (1) Plots the WG density for selected values of parameters α, β, γ and p. Figure (2) shows the β effects while fixing α, γ and p. As same as with Figure (3) γ effects while fixing α, β and p. Figure (4) also presented p effects while fixing α, β and γ.
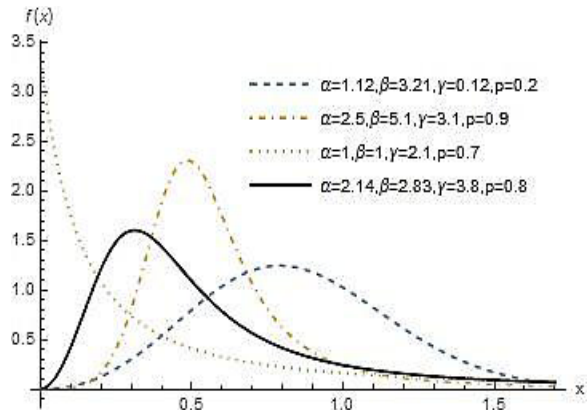
Figure 1: The graph of PDF.

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إمتداد توزيع ويبل الهندسي: خصائص وتطبيق

عظيم علي¹، زهرة سلطان¹، علياء المطيري²*

ملخص البحث: في هذه الدراسة افترض توزيعاً جديداً يسمى امتداد توزيع ويبل-الجيومترك (Extended Weibull-Geometric Distribution). وتم اشتقاق الخصائص المتنوعة من هذا التوزيع، على سبيل المثال: العزوم (Moments)، والانحراف المتوسط (Mean Deviation)، والإحصاءات المرتبة (Order Statistics). وتناقش الدراسة ريناي إنتروبي (Rényie Entropy) وبيتا إنتروبي (Beta Entropy)، وكما أن توزيع المعاملات تم تقديرهم من خلال طريقة مقدر الاحتمال القصوى (Maximum Likelihood) ، وأيضاً مناقشة نموذج المحاكاة (Simulation). وقد ظهرت المرونة والإمكانية للتوزيع الجديد من خلال تطبيق مجموعة بيانات الدراسة من العالم الحقيقي(Real-World Data Set).

* للمراسلة:

(1) قسم الإحصاء، كلية علم الاجتماع، الجامعة الحكومية، لاهور، الرمز البريدي 54000، باكستان.

(2)* قسـم الرياضيــات، كلية العلـوم، جامعة طيبة، المدينــة المنــورة، ص. ب. 41239، الرمز البريدي 41521، المملكة العربية السـعودية.
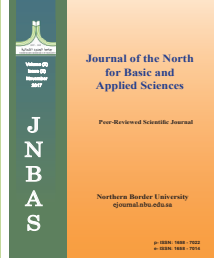
e-mail: amutairi@taibahu.edu.sa

THE EXTENDED WEIBULL-GEOMETRIC DISTRIBUTION: PROPERTIES AND APPLICATION

Azeem Ali [1], Zahra Sultan[1], Alya Al Mutairi [2*]

Abstract: This paper proposes a new model of statistics, namely the Extended Weibull Geometric Distribution (EWGD). Various properties of this distribution are derived, such as moments, mean deviation and order statistics. The study also discusses the Rényie and Beta entropies. The parameters are estimated through the maximum likelihood method; simulation results are provided. The flexibility and potentiality for new distribution are demonstrated through a real-world data set.

* Corresponding Author:
(1) Department of Statistics, Faculty of Social Sciences, Government College University, Lahore, Postal code 54000, Pakistan.
(2)* Department of Mathematics, Faculty of Science, Taibah University, Almadina Almunawwarah, Postal code 41521, P.O. Box 41239, Kingdom of Saudi Arabia.
      e-mail: amutairi@taibahu.edu.sa

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Orlando, A., Refolo, M.G., Messa, C., Amati, L.,

CONCLUSION

In conclusion, kefir is an anti-proliferative agent and an apoptotic agent that induces the killing of cancer cells. The results of this review suggest that kefir may be associated with cancer prevention and that it also has beneficial effects in cancer treatment. This protection may be associated with kefir's bioactive components including peptides, polysaccharides and sphingolipids. The preventive effects of kefir and its product kefiran have been demonstrated to control several types of cancer, including gastric, colon, colorectal, breast, leukemia, and osteosarcoma. The proposed mechanisms of action include antioxidant effects, inhibition of growth-factor signaling, cytokines production, and enhancement of chemotherapy agents. Therefore, Kefir may be used in our daily diet as a prophylactic agent (Figure 1). Future researches are highly recommended to explore the role of using kefir with different chemotherapeutic agents *in vivo*.

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10(+) cells in mammary glands and in tumors and inhibited IL-6(+) cells in tumor.

de Moreno de LeBlanc, Matar, Farnworth, & Perdigón (2007) reported that when mice with breast tumor were fed kefir and KF for 2 or 7 days, they showed different cytokines profiles. Mice fed KF cyclically for 2-days showed changes in CD4+ and CD8+ cells balance in the mammary gland. The CD4+ number increased while CD8+ number remained constant along with an augmentation of the apoptotic cell numbers and decreases in Bcl-2 cell numbers in the mammary gland. The anti-proliferative effects of kefir was studied for 6 days by Chen, Chan, & Kubow (2007) on human mammary cancer cells (MCF-7) and normal human mammary epithelial cells (HMECs). The authors found that kefir inhibited the growth of MCF-7 cell line in a dose-related manner, reporting 29% depression of proliferation at the dose 0.63% and 56% depression at the 2.5% dose. No anti-proliferative effects of kefir extracts were observed in the HMECs. It also has been demonstrated that the anti-proliferative effect of kefir, especially on estrogen dependent cancer cells, is exerted through

the decreases of IL-6, a pro-inflammatory cytokine involved in estrogen synthesis. Thus, the decrease of estrogen level is followed by a decrease in tumor growth. This may be related to kefir constituents that specifically inhibit the growth of human breast cancer cells (de Moreno de LeBlanc *et al.*, 2006 & Chen *et al.*, 2007).

8. OSTEOSARCOMA

Osteosarcoma is a malignant tumor of bone in which there is a proliferation of osteoblasts. Osada, Nagira, Teruya, Tachibana, & Shirahata (1993) demonstrated that kefir contains an active substance that enhances IFN-β secretion of human osteosarcoma line MG-63 when treated with a chemical inducer, poly I: poly C. In addition, kefir contains unique sphingomyelins which can enhance the secretion of IFN-β, an anti-proliferative cytokine.

Figure (1) shows the mechanism of action of kefir in fighting different types of cancer that could be used in our daily diet as a prophylactic agent.
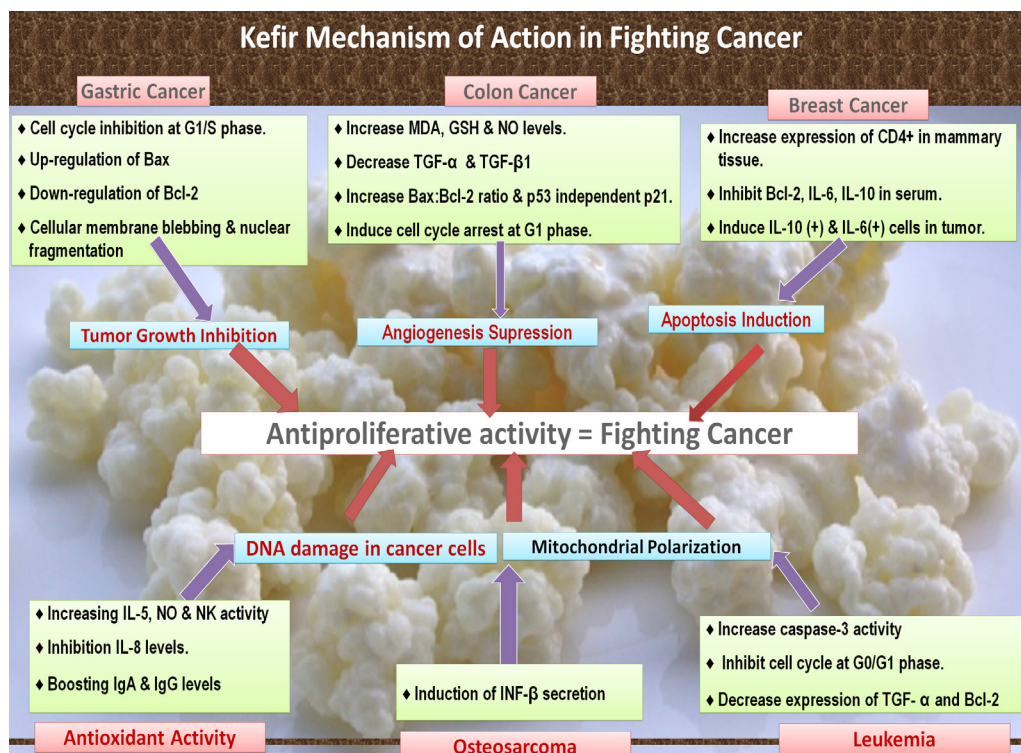

Figure 1: Diagram summarizes the mechanism of action of kefir in fighting different types of cancer.

lymphoblastic leukemia (ALL) is a malignancy type that has an overall recovery rate reached to 85% in children and 40% in adults (Maalouf, Baydoun, & Rizk, 2011). The human T-cell lymphotropic virus type 1 (HTLV-1) is the causative agent of adult T-cell leukemia, which is a fatal disease with no effective treatment (Zimmerman, Niewiesks, & Lairmore, 2010). The maximum cytotoxicity recorded after treatment with 80μg/μL kefir was only 42% and 39% in CEM and Jurkat cells, after 48-hours respectively. CEM cells, a cell line derived from human T cells and Jurkat cells, are an immortalized line of human T lymphocyte cells that are both used to study acute T cell leukemia, T cell signaling, and the expression of various chemokine receptors susceptible to viral entry, particularly HIV (Rizk, Maalouf, & Baydoun, 2009). The anti-proliferative activity of kefir was dose and time-dependent. In CEM and Jurkat cell lines, kefir exhibited its antiproliferative effect by decreasing transforming growth factor-alpha (TGF-α) and upregulating transforming growth factor-beta1 (TGF-β1) mRNA expression. Upon kefir treatment, a marked increase in cell-cycle distribution was noted in the preG(1) phase of CEM and Jurkat cells, indicating the proapoptotic effect of kefir. In conclusion, kefir is effective in inhibiting proliferation and inducing apoptosis of CEM and Jurkat cells which are HTLV-1-negative malignant T-lymphocytes (Rizk *et al.*, 2009; Maalouf *et al.*, 2011). TGFs are a large family of cytokines that have various effects on cells, such as regulating proliferation, differentiation, and apoptosis. TGF-α is a cytokine that induces the proliferation and replication of cells through binding to the epidermal growth factor receptor (EGFR) (Jorissen, Walker, Pouliot, Garrett, Ward, & Burgess, 2003). Binding to EGFR induces autophosphorylation of the receptor, triggering a phosphorylation cascade with some targets binding Src and JAK-2. Another consequence of EGFR-binding is the activation of the proto-oncogene Ras. It has been reported that Ras overexpression may lead to the development of skin papillomas in mice as well as other types of cancer (Harris, Chung, & Coffey, 2003). TGF-β, on the other hand, is a proapoptotic TGF. Saeki, You, Kato, Miyazono, Yazaki, & Takaku (1997) showed that TGF-β led to the induction of cell density-dependent apoptosis in human leukemia HL-60 cells. TGF-β was also

shown to induce Fas-mediated apoptosis in human T-cells (Cerwenka, Kovar, Majdic, & Holter, 1996; Chen, Jin, & Wahl, 1998) and to promote apoptosis in B-cells through the NF-jB/Rel pathway (Patil, Wildey, Brown, Choy, Derynck, & Howe, 2000). The cell-cycle inhibition occurred at the G0/G1 phase as a result of the increase in the number of cells in the Pre-G1 phase. This G0/G1 arrest may also indicate that kefir induces apoptosis in malignant cell lines (Maalouf *et al.*, 2011).

Ghoneum & Gimzewski (2014) examined the apoptotic effect of a probiotics fermentation technology (PFT) of a kefir grain product on human multidrug-resistant (MDR) myeloid leukemia (HL60/AR) cells *in vitro* for 3 days. PFT is a novel natural mixture composed of Lactobacillus kefiri P-IF, a specific strain of *L. kefiri* with unique growth characteristics. HL60/AR cells were cultured with PFT (0.6-5.0 mg/ml). PFT induced apoptosis in HL60/AR cells in a dose-dependent manner, which was maximal at 67.5% for 5 mg/ml. Induction of apoptosis was associated with activation of caspase-3, decreased expression of Bcl-2, and decreased polarization of MMP. In addition, PFT showed a unique characteristic of piercing holes in HL60/AR cells that may be responsible for the apoptotic effect on cancer cells. These results suggest that PFT may act as a potential therapy for the treatment of MDR leukemia (Ghoneum & Gimzewski, 2014).

7. BREAST CANCER

This type of cancer is a malignant proliferation of epithelial cell lining the ducts or lobules of the breast. Breast cancer is still the most common cancer among women (Rebecca & Jemal, 2013). de Moreno de LeBlanc, Matar, Farnworth, & Perdigón (2006) studied the effects of the consumption of kefir or kefir cell-free fraction (KF) for 2 or 7 days on the systemic and local immune responses in mammary glands using a murine hormone-dependent breast cancer model. Mice were subcutaneously injected with tumor cells in the mammary gland. Four days post-injection, they received kefir or KF on a cyclical basis. Both kefir and KF induced IL-10 in serum and depressed IL-6(+) cells that were involved in estrogen synthesis in mammary glands. A two-day administration of KF augmented IL-

(2005) concluded that diluted commercial kefir and pasteurized kefir consumed by BALB/c mice had the ability to boost the mucosal immune system in a dose-related manner.

4. GASTRIC CANCER

Gastric cancer is the third most common cause of cancer-related death in the world (World Health Organization, 2015), and it remains difficult to cure, primarily because most patients are usually diagnosed at an advanced stage of the disease. Human gastric cell line SGC7901 cells were treated with Tibetan kefir, which caused an inhibition in the G1/S phase that induced apoptosis through up-regulation of Bax and down-regulation of Bcl-2 (Gao, Gu, Ruan, Chen, He, & He, 2013). Bax and Bcl-2 both play an important role in acceleration the process of apoptosis (Ibrahim, 2013).

Ghoneum & Felo (2015) showed that *Lactobacillus kefiri* (LK) induced apoptosis in AGS gastric cancer cells in a dose-dependent manner. Apoptosis was detected at a concentration of 0.3 mg/ml (20.8%), increased to 25.8% at 0.6 mg/ml, 37% at 1.2 mg/ml, 53.1% at 2.5 mg/ml, and peaked at 66.3% at 5.0 mg/ml. Apoptosis is associated with the decreased polarization of mitochondrial membrane potential (MMP) and decreased antiapoptotic protein Bcl2 expression. This may result in the release of pro-apoptotic molecules that cause the activation of caspases and eventually lead to apoptosis. LK-treated AGS cells manifested membrane blebbing, nuclear condensation, and fragmentation; hence, it may have the capacity for gastric cancer treatment. The mitochondrial pathway appears to be the main route for the induction of apoptosis against gastric cancer cells by different types of probiotics, such as *L. paracasei* IMPC2.1, and *L. rhamnosus* GG (L.GG) (Orlando, Refolo, Messa, Amati, Lavermicocca, Guerra, & Russo, 2012).

5. COLON CANCER

Colon cancer is the second leading cause of cancer deaths, while colorectal cancer is the third most common cancer worldwide and the third leading cause of cancer mortality in many countries (Parkin & Bray, 2006). Kifer administration caused an increase in malondialdehyde (MDA) level in the stomach, a slight increase in glutathione (GSH) level in colon, and an increase in NO levels in the colon and liver. Cenesiz, Devrim, Kamber, & Sozmen (2008) reported that Kefir has antioxidant activity in mice with colonic aberrant crypts formed by azoxymethane. Kefir composed of high amounts of short chain fatty acids including lactate and acetate can protect cells from DNA damage associated with carcinogenesis via promoting the immune system (Grishina, Kulikova, Alieva, Dodson, Rowland, & Jin, 2011). Short chain fatty acids, by stimulating production of T cells, antibodies and cytokines, have critical roles in immune protection. Also, they improve the barrier properties of the colonic mucosal layer by inhibiting adhesion irritant, which contributes to immune function (Wong, de Souza, Kendall, Emam, & Jenkins, 2006).

Kefir's antitumor activity was also tested on colorectal cancer (CRC) cell lines, Caco2 and HT29. Khoury, El-Hayek, Tarras, El-Sabban, El-Sibai, & Rizk (2014) found that kefir exhibits an antiproliferative effect on Caco2 and HT29 cells. Kefir has the ability to induce cell cycle arrest at the G1 phase, decreasing the transforming growth factor α (TGFα) and transforming growth facto rβ1 (TGFβ1) and p53 independent p21 expression in HT29 cells. Up-regulation in Bax:Bcl2 ratio confirms the proapoptotic effect (Ibrahim, 2013) causing inhibition of proliferation and induction of apoptosis of tumor cells. It was suggested that the observed overexpression of p21, which was seen to be p53-independent, could be the reason for the cell cycle arrest at the G1 phase observed upon kefir treatment. The supernatants of kefir contained high amounts of acetic and lactic acid but only a very small quantity of caproic and butyric acid, and they showed significantly greater antioxidant capacity than milk. These findings suggest kefir can reduce DNA damage, which might be due to their antioxidant capacities by arresting cell cycle at G1 phase (Grishina *et al.*, 2011).

6. LEUKEMIA

The type of leukemia depends on the type of blood cell that has become cancerous. Adult

D-glucose and D-galactose, and is mainly produced by *Lactobacillus kefiranofaciens* (Zajšek *et al.*, 2011; Prado *et al.*, 2015). Kefiran is a water-soluble polysaccharide (Micheli, Uccelletti, Paleschi, & Crescenzi, 1999). It has also been shown to be one of the substances having few or no side effect in functioning to retard tumor growth *in vivo*.

Other bioactive compounds that are found in kefir are serine and glucose or galactose; these molecules could be a sphingolipid compound. The ceramide is a component of sphingolipids that is derived from serine and sphingolipids, such as cerebrosides, that contain either a glucose or galactose. Sphingolipids, such as gangliosides, are sphingosine compounds that contain several glucose or galactose units (Chen *et al.*, 2011). Ceramide has been detected in dairy gangliosides (Colarow, Turini, Teneberg, & Berger, 2003) and cultured dairy products have been shown to be a rich source of gangliosides (Murphy, Dias, & Thuret, 2014). Ceramide is derived from sphingomyelin (SpM) and can act as an intracellular second messenger for tumor necrosis factor-alpha (TNF-α), inteleukin-1beta (IL-1β), and other cytokines (Chen *et al.*, 2011). Ceramide and its analogs, such as C2 and C6, are cell permeable ceramide analogs that have been shown to induce the cell apoptosis of cancer cells (Fillet, Bentires-Alj, Deregowski, Greimers, Gielen, Piette, Bours, & Merville, 2003). Also, Modrak, Cardillo, Newsome, Goldenberg, & Gold (2004) delineated that SpM has been shown to enhance the ceramide formation and ceramide-induced apoptosis when used with gemcitabine (a chemotherapeutic agent), in human pancreatic cancer cells.

3. MECHANISM OF ACTION

Bioactive peptides have been defined as specific protein fragments (Kitts & Weiler, 2003) or peptides with hormones (Fitzgerald & Murray, 2006) that eventually modulate physiological functions through binding to specific receptors on target cells leading to physiological responses. Bioactive peptides possess antimicrobial, antithrombotic, antihypertensive, opioid, immuno-modulatory, mineral binding and antioxidative activities (Fitzgerald & Murray, 2006). All these activities have affirmative actions on body functions for a good health (Kitts & Weiler, 2003). Bioactive peptides found in kefir stimulate innate immunity by activating macrophages, inducing phagocytosis, increasing nitric oxide (NO) and cytokine production and strengthen IgG and IgA+ B-lymphocytes levels (Adiloğlu, Gönülateş, Işler, & Senol, 2013). Kefir use increases the immune response towards Th1 helper cells (pathway for cellular immunity that fight allergy) and decreases Th2 helper cells response (pathway for humoral immunity that fight extracellular organisms) (Kidd, 2003; Adiloğlu *et al.*, 2013). Interleukin-8 (IL-8) inhibition due to consumption of 200 mL kefir daily for 9 weeks controls the inflammatory response by suppressing neutrophil activation and chemotaxis. Adiloğlu *et al.* (2013) also concluded that increased IL-5 stimulate secretory IgA at gastrointestinal mucosa is responsible for more efficient immune response in the intestinal lumen (Adiloğlu *et al.*, 2013).

Kefir consumption for seven consecutive days boosts the immune response in mice by augmenting IgA+ cells number in the intestinal and bronchial mucosa and by increasing the phagocytic activity of peritoneal and pulmonary macrophages. Vinderola, Perdigón, Duarte, Thangavel, Farnworth, & Matar (2006) studied the capacity of the two fractions of kefir (F1: solids including bacteria and F2: liquid supernatant), on the peritoneal macrophages and on the adherent cells from Peyer's patches (as lines for the innate immunity). Both fractions F1 and F2 induced augmentation TNF-α and IL-6 on peritoneal macrophages.

IL-1α on adherent cells from Peyer's patches was enhanced after F1 and F2 feeding except for interferon-gamma (IFN-γ) after F2 administration. Moreover, the percentage of IL-10+cells induced significantly on adherent cells from Peyer's patches after consumption of F2 than F1. Different components of kefir have *in vivo* role as oral biotherapeutic substances capable of stimulating immune cells of the innate immune system to down-regulate the Th2 immune phenotype or to promote cell-mediated immune responses against tumors and intracellular pathogenic infections (Vinderola *et al.*, 2006). In another experiment by Vinderola, Durate, Thangavel, Perdigón, Farnworth, & Matar

1. INTRODUCTION

Fermented beverages and foods have different nutritional and therapeutic properties. Kefir or *keyif* means "feeling good" after its ingestion (Tamime, 2006). It originated in the Balkans, in eastern Europe, and in the Caucasus (Serafini, Turroni, Ruas-Madiedo, Lugli, Duranti, Zamboni, Bottacini, van Sinderen, Maegolles, & Ventura, 2014). Kefir is a unique fermented milk beverage produced by the action of bacteria, yeasts and acetic acid bacteria that stick to a polysaccharide matrix in kefir grains (Chen, Shi, Yang, Nan, Liu, & Wang, 2015). Kefir acts as a matrix in the effective delivery of probiotic microorganisms in different types of products (Prado, Blandón, Vandenberghe, Rodrigues, Castro, Thomaz-Soccol, & Soccol, 2015).

Kefir is manufactured by fermenting milk with commercial freeze-dried kefir starter cultures (Bensmira, Nsabimana, & Jiang, 2010). After fermentation, kefir grains break up to new generation grains that have similar properties as the old ones (Gao, Gu, Abdella, Ruan, & He, 2012). The microbial feature of kefir grains have a steady and specific equilibrium of yeast and lactic acid bacteria which exist in a symbiotic association (Guzel-Seydim, Kok-Tas, Greene, & Seydim, 2011). Kefir has a high nutritional value; it is considered as a good source of calcium and proteins. Fermented milks have many health benefits, such as prevention of gastrointestinal infections, glucose level control, cholesterol inhibition and antitumor activities. Lactose intolerant individuals and patients suffering from atherosclerosis are recommended to use fermented products (de Oliveira Leite, Miguel, Peixoto, Rosado, Silva, & Paschoalin, 2013). Moreover, kefir is a good dietetic beverage; it is of particular interest to athletes and good for feeding small babies and pre-schoolers for good tolerance against disease (Ahmed, Wang, Ahmed, Khan, Nisa, Ahmed, & Afreen, 2013). The regular consumption of kefir enhances the body immune system to fight carcinogenic agents (Ahmed *et al*., 2013).

Kefiran is the main polysaccharide component in kefir, which is mainly produced by *Lactobacillus kefiranofaciens* (Zajšek, Kolar, & Goršek, 2011; Prado *et al*., 2015). The viscosity and viscoelastic properties of acid milk gels are improved by kefiran usage (Rimada & Abraham, 2006). Lactic acid, ethanol and CO_2, are the major products of kefir which confer its beverage viscosity, acidity and low alcohol content. Diacetyl, acetaldehyde, ethyl and amino acids are the minor components that contribute to its flavor (Rattray & O'Connel, 2011).

Regular kefir consumption causes lactose intolerance symptoms inhibition, immune system boosting, lower cholesterol, anti-mutagenic, and anti-carcinogenic activities (Guzel-Seydim *et al*., 2011). Kefiran has memorable features, such as anti-inflammatory (Tamime, 2006), antitumor, antifungal, antibacterial properties (Ahmed *et al*., 2013) immunomodulation or epithelium protection (Serafini *et al*., 2014), and antioxidant activity (Chen *et al*., 2015). *In vitro* studies on breast, colon, skin and gastric cancers and leukemia cell lines and experimental studies on different sarcomas consistently showed valuable effects of kefir on cancer prevention and treatment (Rafie, Golpour Hamedani, Ghiasvand, & Miraghajani, 2015). Administration of soy milk kefirs orally to mice inoculated with sarcoma 180 tumor cells resulted in 70.9% inhibition of tumor growth (Liu, Wang, Lin, & Lin, 2002). In addition, kefir induced apoptotic tumor cell lysis. Mice fed with soy milk kefir for 30 days reported increased levels of total immunoglobulin A (IgA) in the tissue extracted from the wall of the small intestine. These findings suggested that soy milk kefir considered as a promising agent for cancer prevention and boosting the mucosal resistance to gastrointestinal infection (Liu *et al*., 2002).

The target of this review is to explore kefir's mechanism of action in boosting the immune system to fight cancer.

2. KEFIR STRUCTURE

Kefir has a complex mixture composed of peptides, proteins, organic acids and some small molecules, such as free amino acids and oligosaccharides (Chen, Chan & Kubow, 2011). The major components of kefir fractions have antiproliferative activity which is composed of lactose and acetic acid, possibly an end product of fermentation of the milk protein and sugar by the kefir bacteria and yeast.

The lactose polymer may be fragments of previously isolated polysaccharides termed as kefirans. Kefiran, composed of equal proportions of

بحث مرجعي

الكيفير وآلية المقاومة ضد أنواع السرطان المختلفة

أمل عطية المرسي إبراهيم 1*، 2

ملخص البحث: على مر التاريخ، كان الناس دائما مهتمة بالمركبات المستخلصة من مصادر طبيعية مثل المعززات الحيوية للبكتريا، والحيوانية، والنباتية. وقد استخدمت مستخلصات مختلفة من السموم والزهور لعزل المركبات التي يمكن أن تستخدم لأغراض طبية علاجية مختلفة. يعتبر الكيفير أحد منتجات الألبان الشهيرة، والتي تنتج بفعل البكتيريا والخمائر في حبوب الكيفير. الكيفير يحتوي على قيمة غذائية كبيرة بسبب وجود العناصر الغذائية الحيوية مثل البروتينات والكربوهيدرات والمعادن والفيتامينات. وبما أن لكل نوع من أنواع السرطان أسبابه المختلفة، فإن آلية قتال الخلايا السرطانية هي أيضا مختلفة. تأتي آلية القتال المختلفة من اختلاف العقار او المركبات الطبيعية المستخدمة في علاج السرطان. تلخص هذه الدراسة آلية قتال الكيفير المختلفة في علاج بعض أنواع السرطان. ويمكن تلخيص هذه الآلية في حدوث ضرر للحمض النووي للخلايا السرطانية، تحريض الموت المبرمج للخلايا السرطانية، وتثبيط نمو الأورام، انتاج السيتوكينات وتعزيز العلاج الكيميائي. أثبتت هذه الآليات السيطرة على عدة أنواع من السرطان، بما في ذلك سرطان المعدة والقولون، القولون والمستقيم، والثدي، وسرطان الدم، وسرطان العظم. لذلك، يمكن استخدام الكيفير في نظامنا الغذائي اليومي كعامل وقائي.

الكلمات المفتاحية: الكيفير؛ آلية العمل؛ مكافحة السرطان.

* للمراسلة:

(1)* قسم علوم الأحياء، كلية العلوم، جامعة الحدود الشمالية، ص.ب.1321، عرعر 91431، المملكة العربية السعودية.

(2) قسم علم الحيوان، كلية البنات للآداب والعلوم والتربية، جامعة عين شمس، هليوبوليس11757، القاهرة، جمهورية مصر العربية.

e-mail: amal_ai_elmorsy@yahoo.com, & amal.ibrahim@nbu.edu.sa

REVIEW ARTICLE

KEFIR'S FIGHTING MECHANISM AGAINST DIFFERENT CANCER TYPES

Amal Attia El-Morsy Ibrahim[1]*, [2]

Abstract: Over history, people have always been interested in naturally occurring compounds from probiotic, animal, and plant sources. Different extracts of venoms and flowers have been used for isolating compounds that could be used for various purposes. Kefir is a fermented milk renowned dairy product that is produced by the action of bacteria and yeasts in kefir grains. Kefir has a great nutritional value due to the existence of vital nutrients such as proteins, carbohydrates, minerals, and vitamins. As each type of cancer has a different etiology, so the fighting mechanism is also different. The fighting mechanism is different in response to the type of cancer and the type of drug or natural product used to fight. This review reports on kefir's fighting mechanism for the different cancer types. This mechanism can be summerized in damaged DNA of cancer cells, apoptosis induction of tumor cells, and tumor growth inhibition, cytokines production and enhancement of chemotherapy agents. These mechanisms have demonstrated the ability to control several types of cancer, including gastric, colon, colorectal, breast, leukemia, and osteosarcoma. Therefore, Kefir may be used in our daily diet as a prophylactic agent.

* Corresponding Author:

(1)* Department of Biological Sciences , Faculty of Science, Northern Border University, P.O. Box 1321, Arar 91431, Kingdom of Saudi Arabia.

(2) Department of Zoology, Girls' College for Arts, Education and Science, Ain Shams University, Heliopolis 11757, Cairo, Egypt.

e-mail: amal_ai_elmorsy@yahoo.com & amal.ibrahim@nbu.edu.sa

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Correspondence

Editor-in-Chief
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Northern Border University, P.O.Box 1321, Arar 91431,
Kingdom of Saudi Arabia.
Tel: +966(014)6615499
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