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Journal Name:	Journal of Pharmaceutical Research International
Manuscript Number:	**Ms_JPRI_52959**
Title of the Manuscript:	**A Review on Medicinal Plants with Antiangiogenic Activity Available in Iraq**
Type of the Article	

General guideline for Peer Review process:

This journal's peer review policy states that **NO** manuscript should be rejected only on the basis of '**lack of Novelty'**, provided the manuscript is scientifically robust and technically sound.
To know the complete guideline for Peer Review process, reviewers are requested to visit this link:

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PART 1: Review Comments

	Reviewer's comment	**Author's comment** *(if agreed with reviewer, correct the manuscript and highlight that part in the manuscript. It is mandatory that authors should write his/her feedback here)*
Compulsory REVISION comments	**ABSTRACT** 1. Reformat Abstract according to Journal guidelines for authors, For example: • The abstract should be concise and informative. It should not exceed 300 words in length. It should briefly describe the purpose of the work, techniques and methods used, major findings with important data and conclusions. Different sub-sections, as given below, should be used. (see journal website): http://www.journaljpri.com/index.php/JPRI/about/submissions#authorGuidelines • SAMPLE ABSTRACT: • Aims: Here clearly write the aims of this study. Sample: To correlate platelet count, splenic index (SI), platelet count/spleen diameter ratio and portal-systemic venous collaterals with the presence of esophageal varices in advanced liver disease to validate other screening parameters. • Study design: Mention the design of the study here. • Methodology: Please write main points of the research methodology applied. Sample: We included 63 patients (40 men, 23 women; age range 18-75 years) with liver cirrhosis and portal hypertension, with or without the medical history of gastrointestinal bleeding. Clinical as well as hematological examination (platelet count) and ultrasonography (gray as well as color Doppler scale including splenic index and splenorenal/ pancreaticoduodenal collaterals) was done besides upper GI endoscopy for esophageal varices. Platelet count/spleen diameter ratio was also calculated. • Results: Kindly make sure to include relevant statistics here, such as sample sizes, response rates, P-values or Confidence Intervals. Do not just say "there were differences between the groups". sample: Out of 63 patients, 36 patients with small varices (F1/F2) and 27 with larger (F3) varices were detected on endoscope. Significant increase in mean splenic index from low (86.7 +/- 27.4) to high (94.7 +/- 27.7) grade varices was documented. Opposite trend was found with platelets (120.2 +/- 63.5 to 69.8 +/- 36.1) and platelets/ splenic diameter ratio (1676.7 to 824.6) declining significantly. Logistic regression showed splenic collaterals and platelets are significantly but negatively associated with esophageal varices grades. • Conclusion: Non-invasive independent predictors for screening esophageal varices may decrease medical as well as financial burden, hence improving the management of cirrhotic patients. These predictors, however, need further work to validate reliability. 2. Arrange keywords alphabetically INTRODUCTION 3. ~~Natural products have been used for the treatment of different diseases from thousands of years. diverse plants have been used as medicaments in many civilizations in Mesopotamia, Egypt, China, India, and Greece from ancient times and a large number of modern drugs have been developed from them. Records on the medicinal uses of plants appeared in about 2600 BC from the Sumerians and Acadians (1).~~ This information is adequately captured in the 3rd paragraph of Introduction. 4. Paragraph 2: It is important to indicate current synthetic drug treatment and the	

negatives side-effects thereof. This will set the scene for the motivation of research into natural antiangiogenic plant-based products.

5. For additional editorial issues, refer to the accompanied annotated manuscript.
6. "Historically, the best known disorders stemming from angiogenesis are cancer, psoriasis, arthritis and blindness, but many additional common disorders such as obesity, asthma, atherosclerosis and infectious disease are included, and the list is still growing…" - This imply from 2019 onwards – however, your source is 2003) (also if you state the list is growing, then more information from latter date sources should have been included – see also comment below).
7. Table 1 : Diseases characterized or caused by abnormal or excessive angiogenesis (4)
    - The citation [4] comes from 2003, which is 16 (nearly 17) years old [16 year old information is considered extremely old and out-of-date) – surely in the last 16 years newer and more extensive data has also been released. [[4]Carmeliet, P., 2003. Angiogenesis in health and disease. Nature Medicine, 9(6), p.653.
    - It is unprofessional writing to construct a whole Table from just one source – Table must be updated
8. "It has currently (cannot state currently [i.e. 2019] and then cite [[25]. Schoettler & Brahn 2009] – that is 10 years old!! – rephrase sentence) become apparent that angiogenesis plays an important role in its pathophysiology (25)."
9. All abbreviations MUST first be written out in FULL at first mention – correct this throughout the manuscript
10. Obesity - Is all of this from just one source that is 10 years old [[28]Taylor et al. 2009)? – see bullet 2 under item 7.

METHODOLOGY

11. PLEASE refer to the example provided below for how this section should look like - reformat)

    Data Collection
    A literature search was performed regarding the use of indigenous South African medicinal plants on skin to treat fungal diseases. This included all possible sources of information regarding in vivo and in vitro studies regardless of language or publication status (published, unpublished, in press and in progress). Computerized literature searches were performed on MEDLINE, SCOPUS, GOOGLE SCHOLAR, MEDLINE EBSCOHOST and SCIENCE DIRECT databases. In addition, the Global Electronic Thesis and Dissertations (ETD) and South African National ETD were searched for Grey literature. For the retrieval of publications in the databases, the researchers conducted a specific search to define the maximum Medical Subject Headings (MeSH) terms that were related to the research goal. The key terms were "Plant (MeSH)" And "Skin (MeSH)" And "Fungal (MeSH)". In addition to these key words all plants from the South African Pharmacopoeia Monograph project where included in the searches.26 Each plant was searched individually and in conjunction with the aforementioned (MeSH) terms. Further papers were retrieved from reference lists of review articles. Due to the limited number and diversity of studies, including the difficulty to prove comparisons between studies, a meta-analysis was not conducted.

1. **Study selection**

    Inclusion criteria
    Publications that described the use of medicinal plant species (alone or with any combination of South African herbs) indigenous to South Africa to treat fungal skin infections were included in the review. This included in vivo and in vitro studies with

no language restrictions and date limitation.

Exclusion criteria
Non-South African plants (not endemic to South Africa, and imported plants) were excluded. Lastly, viral and bacterial studies were excluded. For studies that included the different types of antimicrobial testing (bacterial, viral and fungal), only the fungal sections where analysed, while the bacterial and viral were omitted.

2. **Selection of data/ reports**
The inclusion of data was assessed by all authors. Discrepancies and disagreements were resolved by consensus among the researchers in several meetings. The first phase of this study was the retrieval of articles based on titles and abstracts of potentially relevant studies in each database. In the second phase the full PDF articles were downloaded and assessed for eligibility. The reference list of review articles was also evaluated in search of other publications of interest not retrieved in the database search in phase 1.

RESULTS

12. **Reformat this paragraph according to the following example:**
In the present study, a total of 67 abstracts were identified from electronic searches. The search identified 62 articles, with 0 from PUBMED, 5 from MEDLINE, 8 from SCOPUS, 29 from GOOGLE SCHOLAR, 8 from SCIENCE DIRECT and 7 from the GLOBAL and SOUTH AFRICAN ETD. An additional 5 articles were retrieved from reference lists of review articles. After the removal of duplicates, as well as screening from relevant titles and abstracts, a total of 49 articles underwent a full text review and 10 articles met the inclusion and exclusion criteria. Table 1 below illustrates the 10 studies selected.

Diversity and distribution of medicinal plants (Example on how this section should be constructed)
Table 2 summaries the results of the literature investigation on medicinal plants used as anti- angiogenesis agents. Here, the botanical names of the species are arranged in alphabetical order along with their local name, family, part used, region in South Africa, part used and in vitro testing. In this study, 15 indigenous plant species distributed in eight families and eleven genera were identified as being used to treat one or more fungal skin infections. The medicinal plant species are distributed across eight South African provinces (excluding North West). About 13 (86,7%) plants were found in the Eastern Cape, with 10 (66.7%) in the Western Cape and Kwa-Zulu- Natal, 9 (60%) in Mpumalanga, 6 (40%) in Northern Cape, 2 (13%) in Limpopo and Free State and only one (6.7%) found in Gauteng.

These results show that the majority of the 15 plant species belonged to families located within or in some parts of the Eastern & and Western Cape provinces. This could be attributed to the Cape floristic region found within the two provinces. The region is known as a biodiversity hotspot. It hosts almost 20% of all flora on the African continent. South Africa is known to house over 3,000 species with many medicinal uses found across the country.

13. Start this paragraph: Ten plant species from 10 families were found (Table 2).
14. Table 2: List scientific names alphabetically & reorder the next section accordingly (also alphabetically)
15. Species description
    - Typeset all scientific names of plant species in italics
    - Remove all information that is not strictly related to the species being an antiangiogenic agent.
    - Remove family name as it has already been indicated in Table 1 above –

	thus duplication – all duplications to be removed ADD THE FOLLOWING SECTIONS **ACKNOWLEDGMENTS** A brief acknowledgment section may be given after the conclusion section just before the references. The acknowledgments of people who provided assistance in manuscript preparation, funding for research, etc. should be listed in this section. All sources of funding should be declared as an acknowledgment. Authors should declare the role of the funding agency, if any, in the study design, collection, analysis and interpretation of data; in the writing of the manuscript. If the study sponsors had no such involvement, the authors should so state. **COMPETING INTERESTS** Declaration of competing interest is compulsory. All authors must disclose any financial and personal relationships with other people or organizations that could inappropriately influence (bias) their work. Examples of potential conflicts of interest include employment, consultancies, honoraria, paid expert testimony, patent applications/registrations, and grants or other funding. If no such declaration has been made by the authors, SDI reserves to assume and write this sentence: "Authors have declared that no competing interests exist.". **AUTHORS' CONTRIBUTIONS** Authors may use the following wording for this section: " 'Author A' designed the study, performed the statistical analysis, wrote the protocol, and wrote the first draft of the manuscript. 'Author B' and 'Author C' managed the analyses of the study. 'Author C' managed the literature searches…… All authors read and approved the final manuscript." **REFERENCES** **All references should follow the following style:** Reference to a journal: For Published paper: 1. Hilly M, Adams ML, Nelson SC. A study of digit fusion in the mouse embryo. Clin Exp Allergy. 2002;32(4):489-98. Note: List the first six authors followed by et al. Note: Use of DOI number for the full-text article is encouraged. (if available). Note: Authors are also encouraged to add other database's unique identifier (like PUBMED ID). For Accepted, unpublished papers. Same as above, but "In press" appears instead of the page numbers. 1. Saha M, Adams ML, Nelson SC. Review of digit fusion in the mouse embryo. J Embryol Exp Morphol. 2009;49(3): (In press). Note: List the first six authors followed by et al. Note: Use of DOI number is encouraged (if available). Note: Authors are also encouraged to add other database's unique identifier (like PUBMED ID).	

	For Articles not in English Forneau E, Bovet D. Recherches sur l'action sympathicolytique d'un nouveau dérivé du dioxane. Arch Int Pharmacodyn. 1933;46:178-91. French. Reference to a book: Personal author(s) Rang HP, Dale MM, Ritter JM, Moore PK. Pharmacology. 5th ed. Edinburgh: Churchill Livingstone; 2003. Editor(s) or compiler(s) as authors Beers MH, Porter RS, Jones TV, Kaplan JL, Berkwits M, editors. The Merck manual of diagnosis and therapy. 18th ed. Whitehouse Station (NJ): Merck Research Laboratories; 2006. Authored chapter in edited publication Glennon RA, Dukat M. Serotonin receptors and drugs affecting serotonergic neurotransmission. In: Williams DA, Lemke TL, editors. Foye's principles of medicinal chemistry. 5th ed. Philadelphia: Lippincott Williams & Wilkins; 2002. Reference to Web-resource or Electronic articles. Hugo JT, Mondal SC. Parallels between tissue repair and embryo morphogenesis: a conceptual framework. Global Health. 2006;16:4. Accessed 29 March 2012. Available: http://www.globalizationandhealth.com/content/1/1/14. Anonymous. Parallels between tissue repair and embryo morphogenesis: a conceptual framework. Global Health. 2006;16:4. Accessed 29 March 2012. Available: http://www.globalizationandhealth.com/content/1/1/14. Reference to Organization as author Diabetes Prevention Program Research Group. A study of digit fusion in the mouse embryo. J Embryol Exp Morphol. 2009;49(2):259–276**.**	
Minor REVISION comments		
Optional/General comments	The paper is extremely superficial in the presentation of: **Introduction**: The impact of current synthetic drug treatment and the negatives side-effects thereof. **Methodology**: Not presenting enough information to suggest robust reproducibility of results. See above for example on how this section can be beefed up. **Results**: species information as related to their possible action as Antiangiogenic agents. **References**: some too old to be of value **Bibliography** not following journal guidelines.	

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PART 2:

	Reviewer's comment	**Author's comment** *(if agreed with reviewer, correct the manuscript and highlight that part in the manuscript. It is mandatory that authors should write his/her feedback here)*
Are there ethical issues in this manuscript?	*(If yes, Kindly please write down the ethical issues here in details)*	

Reviewer Details:

Name:	***Martin Potgieter***
Department, University & Country	***University of Limpopo, South Africa***