



Evaluation of Antioxidant Property of Moringa Oleifera Leaves and its Effectiveness Against Rheumatoid Arthritis

Manas Jyoti Kapil^{1*}, Dhiren Deka², Mangala Lahkar³ and Neelakshi Sharma¹

¹Pratiksha Institute of Pharmaceutical Sciences, India.

²Govt. Ayurvedic College, India.

³Guwahati Medical College and Hospital, India.

Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

Article Information

DOI: 10.9734/JPRI/2021/v33i41B32358

Editor(s):

(1) Dr. Mohamed Fawzy Ramadan Hassani, Zagazig University, Egypt.

Reviewers:

(1) Tugay Ayasan, Osmaniye Korkut Ata University, Turkey.

(2) Kasta Gurning, Sekolah Tinggi Ilmu Kesehatan Senior Medan, Indonesia.

(3) P Nitya Jeeva Prada, Acharya Nagarjuna University, India.

Complete Peer review History: <https://www.sdiarticle4.com/review-history/72426>

Original Research Article

Received 10 June 2021

Accepted 14 August 2021

Published 23 August 2021

ABSTRACT

The present study is performed with the purpose of evaluating the antioxidant nature of Moringa Oleifera leaves and the effectiveness of the leaf extract against the disease called Rheumatoid Arthritis. The disease is very chronic and it is a common disease. So the study is focused on the medicinal properties of Moringa Oleifera leaves, chemical composition of Moringa Oleifera leaves and seeds, the antioxidant nature of moringa leaves and its extracts, the effectiveness of moringa leaf extract against the Rheumatoid Arthritis disease, reason behind the effectiveness of moringa leaves and discussion and analysis of the result generated.

Keywords: Antioxidant nature; Chemical composition; Moringa Oleifera leaves; Rheumatoid Arthritis.

1. INTRODUCTION

'Moringa Oleifera' is a well known plant for its benefits in the health and medical department. In

this evaluation paper, the antioxidant activity of M. Oleifera will be discussed as the extract of leaves of this tree has a very antioxidant property. The antioxidant property of any plant

leaves is beneficial to reduce the effects of 'rheumatoid arthritis. As the disease, 'Rheumatoid Arthritis' is such a disease which cannot be cured with using medicine but the pain of this disease can be reduced. There is some medicine and physiotherapy which can reduce or slow the progression of 'Rheumatoid Arthritis. The discussion of a paragraph of this journal is about the medical properties of 'Moringa Oleifera' leaves. 'M. Oleifera' is an arboreal tree and it has leaves, fruits, branches and trunk [1]. The leaves of this tree are very small and compound leaves but it has the most benefits compared to the other parts of this tree. Chemical composition of 'M. Oleifera' leaves are not similar to the other leaves and it has some different chemical composition which is antioxidant and not available in other leaves. This makes the tree more identifiable among the medical and health department. The effectiveness of 'M. Oleifera' leaves is very significant and it has been discussed in this journal. The research paper of this journal is very useful for the doctors, medical students as well as the patients who have this disease.

2. MEDICINAL PROPERTIES OF MORINGA OLEIFERA LEAVES

'Moringa Oleifera' is the scientific name of a drumstick tree. The drumstick tree is well known to everyone and it is also known as the miracle tree as the medical benefits of this tree are many. Drumstick is also used as a vegetable and many doctors recommend this vegetable for diabetes patients. The flowers of this tree are also used as vegetables and it is eaten fried. The 'Moringa Oleifera tree' is also known as the bean oil tree [2]. The extract of the leaves of this tree have been used since ancient times for its health benefits and medicinal properties. It has many properties such as antifungal, antioxidant, antiviral, and antidepressant. This tree is native to Indian subcontinent and it is mostly seen in India. 'Moringa Oleifera' also grows in other Asian countries and also in Africa, North America and South America. The fruits of 'Moringa Oleifera' contain various vitamins and proteins [2]. The leaves of 'Moringa Oleifera' contain minerals and vitamins. The leaves of 'Moringa Oleifera' are rich in various vitamins such as vitamin A, vitamin C, various minerals such as calcium, iron, zinc, potassium and magnesium.

The seeds of this tree can be extracted as oil and the oil of 'Moringa Oleifera' seeds are very beneficial to keep hair healthy and clean. The

seeds oil of 'Moringa Oleifera' is also rich in protein and it is very essential and beneficial for the hairs. Protein is also useful for the prevention of damage in skin cells and the damage of hair. Thus hair fall can be treated by using this seed oil.

Extract of moringa leaves can be used to treat edema as the the leaves of 'Moringa Oleifera' have anti inflammatory activities which can be very beneficial to reduce the inflammation of 'Edema' [3]. The extract of leaves can also be used for treatment of cancer. Many doctors have suggested that the leaves of 'Moringa Oleifera' contain a chemical composition called niazimicin. It is believed that the compound can suppress the increase of cancer cells. The extract of leaves also has the properties of antibacterial and antifungal. Various skin diseases which are caused by bacteria and fungus can be cured by applying the extracts on the affected area of skin. The leaves and fruits of 'Moringa Oleifera' are rich in calcium and phosphorus. Calcium and phosphorus are the main constituents of bones [4]. That means to keep the bones healthy and strong, the fruits and leaves of the 'Moringa Oleifera' tree can be eaten.

3. CHEMICAL COMPOSITION OF MORINGA OLEIFERA LEAVES AND ITS IMPACT ON RHEUMATOID ARTHRITIS

Plants are used for medical treatment for a long time. All civilizations have used plants as the cure of various diseases. The modern generation is using the plants by researching on it. The scientists of this generation are researching various plants to know their chemical composition. The chemical composition of plants is used to clarify the medicinal benefits of the plants. Every plant has different chemical composition but every part of the plant has the same chemical composition. Also it may be different sometimes, which is a subject of study and can be beneficial in the generation of better results overall. Drugs are mainly originated from naturally or chemically. The use of drugs which are generated synthetically are extremely dependent on the chemical composition of that particular drug and is designed to meet treatment needs. The natural drugs are more beneficial than the chemical ones and it is believed that the drugs named DMARDs originated from the extract of leaves of 'Moringa Oleifera' trees [5].

There are 16 chemical compositions in 'Moringa Oleifera' which are used as medical treatment. A chemical compound named '9-octadecenoic acid' is present in both fruits and leaves of the trees and it is present about 20 percent. There are 20 percent '2, 6-ascorbic acid- dihexadecanoate' and eight percent of '14-methyl-8-hexadecenal' in the leaves. These three components are highly present in the 'Moringa Oleifera'. There are another 13 components but the density of those components is lower than these three components. Another component which is present about seven percent is '4-hydroxy-4-methyl-2-pentanone' [6]. '3-ethyl-2, 4-dimethylpentane' and 'phytol' are present about six percent and four percent respectively. There are two and half percent of '1, 2-benzene dicarboxylic acid' and one and half percent of 'octadecamethyl-cyclononasiloxane' present in 'Moringa Oleifera'. '3, 4-epoxyethane' and 'N-(-1-methylethylidene)-benzene ethanamine' are comprised about 1.50% each in 'Moringa Oleifera'.

There are present '4, 8, 12, 16-tetramethylheptadecan-4-olide' about 2.70 percent and '3-5-bis (1, 1-dimethylethyl)-phenol' is about 2.50 percent in 'Moringa Oleifera' [7]. The component '3, 7, 11, 15-tetramethyl-2 hexadecene-1-ol' is also present in 'Moringa Oleifera' which is about 1.10 percent. 'hexadecanoic acid' and '1, 2, 3-propanetriyl ester-9 octadecenoic acid' are present about 1.20 and 1.80 percent respectively in the tree. The oil of seed extract has oleic acid about 85 percent and it is mainly the rich component of seeds oil. 'L-(+) -ascorbic acid- 2, 6-dihexadecanoate' and 9-octadecenoic acid' are also present in the seeds oil which is about 10 percent and 1.80 percent respectively. There is a component named 'methyl ester-hexadecanoic acid' which is present in the seeds oil of 'Moringa Oleifera' by 1.30 percent and it is a very rare component. The component, '9-octadecenamamide' is also present in the seeds oil of the tree [8]. This component is present in the leaf extract by 20 percent but in seeds oil about 0.78 percent only.

4. ANTI-OXIDANT NATURE OF MORINGA OLEIFERA LEAVES AND ITS USE IN MEDICAL SPHERE

Antioxidants are the components which prevent oxidation and reduce free radicals in the body. Free radicals can induce many pathogenesis which can generate disease such as Rheumatoid

Arthritis, cancer, carcinogenesis, diabetes, cardiovascular attack, inflammatory and many more. Antioxidants help to reduce these free radicals and reactive oxygen [9]. Reactive oxygen can be very toxic and harmful if it has been produced extra than necessary in the human body. The reactive oxygen is produced in the human body constantly but the overproduction of it can cause injuries and diseases. The imbalance of the immune system in the human body can also be caused by the overproduction of reactive oxygen. The free radicals and reactive oxygens are very harmful for the body as it helps the virus and bacteria to attack the body. Therefore it is very necessary to reduce the free radicals and reactive oxygens from the body.

Antioxidants can be found in high quantities in the leaf extract of 'Moringa Oleifera' tree or drumstick tree. Vitamin C is also an antioxidant and it can be found in high amounts in the leaf extract and fruits of 'Moringa Oleifera' [10]. Therefore the use of the tree in medical research centres is increasing day by day. A compound named 'Quercetin' is a powerful antioxidant which can be found in 'Moringa Oleifera'. This compound helps to reduce blood pressure and chronic pain of 'Rheumatoid Arthritis'. Chlorogenic acid is another compound which can be found in 'Moringa Oleifera' and it is also an important antioxidant as it has the ability to reduce the free radicals and reaction of oxygen's in the human body. This is also a medicinal compound and it can reduce the blood sugar levels. The patients who have the diseases such as diabetes, high blood pressure and high blood sugar can use 'Moringa Oleifera' which will be beneficial for the patients [11]. Phenolic compounds can be found in high amounts in 'Moringa Oleifera' which is also an antioxidant compound and it can reduce the risk of various diseases which are caused by free radicals. Phenolic compounds have an effectiveness of reducing the free radicals and reactive oxygens.

The 'Moringa Oleifera' is also rich in flavonoids and it is also a powerful natural antioxidant and it is also used in producing antioxidant medicine by various reputed medicine company such as Centaur Labs, Cipla, Sun pharma, Ranbaxy and they are producing high value antioxidant medicine such as Ocufee Capsule, Ocuguard tablet, Heptagon tablets and Casera tablet. Garlic acid and Kaempferol are another two antioxidants which are found in 'Moringa Oleifera'. So, the drumstick or 'Moringa Oleifera'

is an rich antioxidant and it can be used for reducing the free radicals and reactive oxygens in the human body [12]. The antioxidant nature of 'Moringa Oleifera' makes the tree popular and significant in various medicinal research centres and thus the name of this tree is 'miracle tree' as it is justified to the 'Moringa Oleifera'.

5. EFFECTIVENESS OF MORINGA OLEIFERA LEAVES AGAINST RHEUMATOID ARTHRITIS

The disease 'Rheumatoid Arthritis' is an inflammatory disorder which can be characterised by joint inflammation, synovial growth and articular cartilage degradation. This disease is one of the most prevalent autoimmune illnesses and it is mainly caused by the increase of free radicals in the body continually. 'Rheumatoid Arthritis' is a chronic and progressive sickness of systematic inflammatory. This sickness affects the synovial joints of bones in the human body and it usually results in symmetrical arthritis which causes deformity and impairment. It is a very common disease in India and Africa. Joint pain and damage are the main symptoms of this disease [13]. The disease has 4 stages and it is not curable. In the first stage the body attacks the joint tissue and it is mistakenly occurred by the body. In this stage,

antioxidants are very useful to reduce the pain. 'Moringa Oleifera' is rich in antioxidants; therefore it will be very useful to prevent the disease from spreading to other areas of the body. As the fruits of the trees are used as vegetables, doctors suggest eating drumsticks in the first stage of 'Rheumatoid Arthritis'.

The disease can only be cured in the first stage by reducing the free radicals and reactive oxygens from the body. The free radicals and reactive oxygens can absorb serum from bones and decay the bones of the human body. The second stage of the disease makes antibodies in the body and it causes swollen joints and warms the joints. Extra inflammation of joints isocurred in the second stage of the disease. The areas of the disease can be skin, eyes, salivary glands, nerve tissues, bone marrow, heart, lungs, kidneys, blood vessels and many other regions of the body. In maximum cases the areas are skin and bone marrow. The extract of the leaves of 'Moringa Oleifera' can be massaged in the skin to reduce the inflammation over the skin. There are many antioxidants in 'Moringa Oleifera' such as quercetin, flavonoids, garlic acids and kaempferol which can be very effective to reduce the chronic pain of Rheumatoid Arthritis in the affected zone of the body.

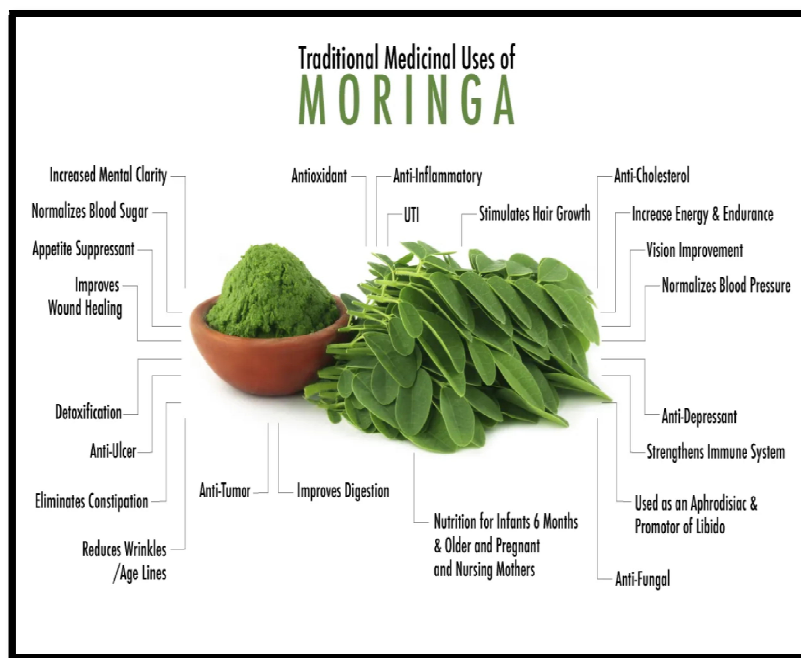


Fig. 1. Importance of Moringa Oleifera

The third stage of the disease is very critical as the joints of bones become bent and deformed. The symptoms are fully visible in this stage. The fourth stage is more critical and toxic than the third stage as the joints become fused. The power of joints becomes decreasing and the body cannot afford the mass of the affected areas [14]. There are many vegetables which are rich in vitamin C and many other antioxidants but many research foundations have approved the effectiveness of 'Moringa Oleifera' as the most effective plant to cure the Rheumatoid Arthritis. The seeds oil of 'Moringa Oleifera' also contains many antioxidants and it is also very useful and effective against the disease named Rheumatoid Arthritis as the antioxidants present in the seed oil is also powerful to scavenge the free radicals.

6. REASONS FOR EFFECTIVENESS OF THE LEAVES IN TREATING THE DISEASE

Arthritis is mainly caused by the increasing amount of free radicals and gasses in the body. Many diseases can be created in the body by gathering extra amounts of free radicals and gases in the body continually for a long time. Antioxidants can reduce the free radicals and gases from the body. The human body is automatically generating reactive oxygen species in the body. Antioxidants can slow the process of generating reactive oxygen in the body. Chemically produced antioxidants have many side effects and it can cause many diseases in the body. Many patients also take antioxidants from medical stores which are produced with chemical components. Excessive use of those antioxidants can cause various panic and disease in the body. Moringa is a natural antioxidant and the use of leaves of the tree in medicine research organizations is increasing [15]. Therefore the Moringa tree is very effective in preventing Arthritis. Moringa leaf powder can be produced by extracting the leaves and drying it. The powder is very effective in regulating oxidative stress.

The blood sugar and cholesterol level can be reduced by mixing powder in milk or water and drinking it. Increasing blood sugar and cholesterol in the blood of the human body is another cause of Arthritis disease. Horseradish leaf powder reduces the blood sugar level and cholesterol level in a significant amount, which means that it is very useful and effective to treat Arthritis. The lipid and glucose level are the other key reasons for Arthritis as the increasing of

glucose level and lipid level in the body can cause arthritis. The leaf powder of Moringa helps the body to maintain the glucose levels and lipid levels in the body. Moringa is a rich source of vitamins, proteins, minerals and amino acids. Ascorbic acids, polyphenols and flavonoids are some powerful antioxidants which are present in Moringa. Moringa can prevent the fusing of joints, damage of joints, warming of joints and decaying in bones which are the basic symptoms of Arthritis. The powder can be mixed in milk and tea to drink as it can be enjoyed as a tea with a slightly earthy taste. The seeds of Moringa also can be chewed every day to reduce the free radicals from the body and it has no side effects to create hazards for the body [16]. That's the reason why Moringa has the highest effectiveness in the treatment of Arthritis among all the plants.

7. DISCUSSION OF THE RESULTS GENERATED

A phytochemical analysis has been done with the extract of Moringa leaves which results that there was presence of alkaloids, flavonoids, glycosides, tannins and saponins. These are the antioxidants which are found in the leaf extract of Moringa. These antioxidants are found in the ethanolic extracts of Moringa Oleifera. The extract was tested by mixing various chemicals with different different samples of Moringa leaf extracts.

An experimental procedure which is used as widely is the anti arthritic procedure of rats. In this experiment, many rats were used to test the power and effectiveness of Moringa leaf powder. Formaldehyde was used to induce arthritis in the body of rats [17]. Formaldehyde can increase the inflammation of edema in rats. Formaldehyde was injected to some rats and it showed significant inflammation in the edema of those rats. The ethanolic extract of moringa leaves had been injected to the rats to see the results. The results have been shown to reduce inflammation of edema to those rats which were injected with moringa leaf extract. The rats which were not injected with the extracts have increased inflammation [18].

This experiment proved that the extract of moringa leaf can reduce the inflammation of Arthritis along with other symptoms such as joint pain, fuse of bone marrow, absorption of serum, decaying of bones. These are the most widely associated diseases associated with the same,

which means that the overall use of the leaves can be extremely beneficial. Besides, it can be helpful in generating the best results associated with the same. There are some side effects of Moringa leaf extracts which had been found after the experiments. Moringa leaf extract has anti fertility quality and thus it is not recommended to pregnant women. The anti-fertility quality of Moringa can reduce the possibility of pregnancy also. Therefore too much consuming of Moringa leaf extract can be harmful for pregnant women [19]. Hence, the discussion over the results proved that Moringa Oleifera has the antioxidant properties and it is really effective against Rheumatoid Arthritis. The properties associated with the leaves are extremely effective, which makes it one of the most important treatments for the same.

8. CONCLUSION

Throughout the study, it can be concluded that Moringa Oleifera has the most effectiveness against the arthritis disease as it has the anti oxidants components. Another name of Moringa Oleifera is miracle tree and the name is purely justified by the benefits of the trees. There are some risks which have to be taken care of. Many patients use the extract to aid thyroid problems and they take it with other thyroid medication. It is true that Moringa leaf contains the compounds which can aid thyroid disease but it should not be taken with other medicines of thyroid disease. This can cause a disease called Levothyroxine. The diabetes patients also use moringa leaf powder as it is very powerful to reduce the blood sugar. But a sufficient amount of blood sugar is needed for the body and too much consuming of moringa leaf extract can reduce the blood sugar to very low. This can give the same effect to reduce blood pressure. The antioxidants property of moringa leaf extracts and moringa seeds oil is very useful for Rheumatoid Arthritis along with other chronic diseases.

DISCLAIMER

The products used for this research are commonly and predominantly use products in our area of research and country. There is absolutely no conflict of interest between the authors and producers of the products because we do not intend to use these products as an avenue for any litigation but for the advancement of knowledge. Also, the research was not funded by

the producing company rather it was funded by personal efforts of the authors.

CONSENT

It is not applicable.

ETHICAL APPROVAL

It is not applicable.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES

1. Vergara-Jimenez M, Almatrafi MM, Fernandez ML. Bioactive components in Moringa Oleifera leaves protect against chronic disease. *Antioxidants*. 2017;6(4):91. Available:<https://www.mdpi.com/2076-3921/6/4/91>
2. Jacques AS, Arnaud SS, Fr&ejus OO, Jacques DT. Review on biological and immunomodulatory properties of Moringa Oleifera in animal and human nutrition. *Journal of Pharmacognosy and Phytotherapy*. 2020;12(1):1-9. Available:<https://pdfs.semanticscholar.org/1d4e/9b71b4426215b384eb1e7cbe6211b8ea880a.pdf>
3. Fahey JW, Wade KL, Stephenson KK, Shi Y, Liu H, Panjwani AA, Olson ME. A strategy to deliver precise oral doses of the glucosinolates or isothiocyanates from Moringa Oleifera leaves for use in clinical studies. *Nutrients*. 2019;11(7):1547. Available:<https://www.mdpi.com/2072-6643/11/7/1547>
4. Khalil SR, El Bohi KM, Khater S, Abd El-fattah AH, Mahmoud FA, Farag MR. Moringa Oleifera leaves ethanolic extract influences DNA damage signaling pathways to protect liver tissue from cobalt-triggered apoptosis in rats. *Ecotoxicology and Environmental Safety*. 2020;200:110716. Available:<https://www.sciencedirect.com/science/article/pii/S0147651320305558>

5. Kou X, Li B, Olayanju JB, Drake JM, Chen N. Nutraceutical or pharmacological potential of Moringa Oleifera Lam. *Nutrients*. 2018;10(3):343.
Available: <https://www.mdpi.com/2072-6643/10/3/343>
6. Falowo AB, Mukumbo FE, Idamokoro EM, Lorenzo JM, Afolayan AJ, & Muchenje V. Multi-functional application of Moringa Oleifera Lam. in nutrition and animal food products: A review. *Food research international*. 2018;106:317-334.
Available: <https://www.sciencedirect.com/science/article/pii/S0963996917309432>
7. Dhakad AK, Ikram M, Sharma S, Khan S, Pandey VV, Singh A. Biological, nutritional, and therapeutic significance of Moringa Oleifera Lam. *Phytotherapy Research*. 2019;33(11):2870-2903.
Available: <https://onlinelibrary.wiley.com/doi/abs/10.1002/ptr.6475>
8. Lin M, Zhang J, Chen X. Bioactive flavonoids in Moringa Oleifera and their health-promoting properties. *Journal of functional foods*. 2018;47:469-479.
Available: <https://www.sciencedirect.com/science/article/pii/S1756464618303074>
9. Moodley JS, Krishna SBN, Pillay K, Govender P. Green synthesis of silver nanoparticles from Moringa Oleifera leaf extracts and its antimicrobial potential. *Advances in Natural Sciences: Nanoscience and Nanotechnology*. 2018;9(1):015011.
Available: <https://iopscience.iop.org/article/10.1088/2043-6254/aaabb2/meta>
10. Villarruel-López A, López-de la Mora DA, Vázquez-Paulino OD, Puebla-Mora AG, Torres-Vitela MR, Guerrero-Quiroz LA, Nuño K. Effect of Moringa Oleifera consumption on diabetic rats. *BMC complementary and alternative medicine*. 2018;18(1):127.
Available: <https://link.springer.com/content/pdf/10.1186/s12906-018-2180-2.pdf>
11. El-Hack A, Mohamed E, Alagawany M, Elrys AS, Desoky ESM, Tolba H, Swelum AA. Effect of forage *Moringa Oleifera* L. (moringa) on animal health and nutrition and its beneficial applications in soil, plants and water purification. *Agriculture*. 2018;8(9):145.
Available: <https://www.mdpi.com/2077-0472/8/9/145>
12. Villasenor-Basulto DL, Astudillo-Sanchez PD, del Real-Olvera J, Bandala ER. Wastewater treatment using Moringa Oleifera Lam seeds: A review. *Journal of Water Process Engineering*. 2018;23:151-164.
Available: <https://www.sciencedirect.com/science/article/pii/S2214714418300990>
13. Saa RW, Fombang EN, Ndjantou EB, Njintang NY. Treatments and uses of Moringa Oleifera seeds in human nutrition: A review. *Food science & nutrition*. 2019;7(6):1911-1919.
Available: <https://onlinelibrary.wiley.com/doi/abs/10.1002/fsn3.1057>
14. Aisida SO, Madubuonu N, Alnasir MH, Ahmad I, Botha S, Maaza M, Ezema FI. Biogenic synthesis of iron oxide nanorods using Moringa Oleifera leaf extract for antibacterial applications. *Applied Nanoscience*. 2020;10(1):305-315.
Available: <https://link.springer.com/article/10.1007/s13204-019-01099-x>
15. McInnes IB, Schett G. Pathogenetic insights from the treatment of rheumatoid arthritis. *The Lancet*. 2017;389(10086):2328-2337.
Available: <https://www.sciencedirect.com/science/article/pii/S0140673617314721>
16. Conigliaro P, Triggianese P, De Martino E, Fonti GL, Chimenti MS, Sunzini F, Perricone R. Challenges in the treatment of rheumatoid arthritis. *Autoimmunity reviews*. 2019;18(7):706-713.
Available: <https://www.sciencedirect.com/science/article/pii/S1568997219301107>
17. Drosos AA, Pelechas E, Voulgari PV. Rheumatoid arthritis treatment. A Back to the drawing board project or high expectations for low unmet needs?. *Journal of clinical medicine*. 2019;8(8):1237.
Available: <https://www.mdpi.com/2077-0383/8/8/1237>
18. Yap HY, Tee SZY, Wong MMT, Chow SK, Peh SC, Teow SY. Pathogenic role of immune cells in rheumatoid arthritis: implications in clinical treatment and biomarker development. *Cells*. 2018;7(10):161.
Available: <https://www.mdpi.com/2073-4409/7/10/161>

19. Taylor PC, Weinblatt ME, Burmester GR, Rooney TP, Witt S, Walls CD, Takeuchi T. Cardiovascular safety during treatment with baricitinib in rheumatoid arthritis. *Arthritis & Rheumatology*. 2019;71(7):1042-1055. Available: <https://onlinelibrary.wiley.com/doi/abs/10.1002/art.40841>

© 2021 Kapil et al.; This is an Open Access article distributed under the terms of the Creative Commons Attribution License (<http://creativecommons.org/licenses/by/4.0>), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

Peer-review history:
The peer review history for this paper can be accessed here:
<https://www.sdiarticle4.com/review-history/72426>