EUROPEAN ACADEMIC RESEARCH
Vol. VII, Issue 2/ May 2019

Impact Factor: 3.4546 (UIF)
DRJI Value: 5.9 (B+)

ISSN 2286-4822
1

Determination of Antibacterial, Antifungal and Antileishmanial Activities in Medicinal Plants and their Impacts on Human Life (A Review)

ATTA UR REHMAN
M.Phil. Scholar
Institute of Biochemisty, University of Balochistan, Quetta, Pakistan
MUHAMMAD ANWAR PANEZAI
Professor, Institute of Biochemistry, University of Balochistan, Quetta
Pakistan
MUDASSIR ASRAR
Professor, Department of Botany, University of Balochistan, Quetta, Pakistan
JAHANGIR KHAN ACHAKZAI
Ph.D. Scholar, Institute of Biochemistry, University of Balochistan, Quetta
Pakistan
ABDUL MANAN KAKAR
Ph.D. Scholar**,** Institute of Biochemistry, University of Balochistan, Quetta
Pakistan
NAZIMA YOUSAF KHAN
Ph.D. Scholar, Institute of Biochemistry, University of Balochistan, Quetta
Pakistan
AJAB KHAN TAREEN
Ph.D. Scholar, Institute of Biochemistry, University of Balochistan, Quetta
Pakistan
MUHAMMAD SULEMAN
M.Phil. Scholar, Institute of Biochemistry, University of Balochistan, Quetta
Pakistan
ABDUL BAQI
M.Phil. Scholar, Department of Chemistry, University of Balochistan, Quetta
Pakistan
INAYATULLAH
M.Phil. Scholar, Institute of Biochemistry, University of Balochistan, Quetta
Pakistan
HAKEEMULLAH
M.Phil. Scholar, Institute of Biochemistry, University of Balochistan, Quetta
Pakistan
ZAHOOR AGHA
M.Phil. Scholar, Institute of Biochemistry, University of Balochistan, Quetta
Pakistan

Abstract:

Medicinal plants include various beneficial compounds which are used in herbal medicine. The early life of human history fully depended on herbs and herbal therapy. The ancient herbalists believed that herbs were the only solutions to cure different chronic and acute diseases. Since then, studies and research on plants metabolites got huge importance to overcome health issues in human and animals. Moreover, with the passage of time synthetic drugs were introduced in medicinal world that had the ability to cure health immediately. However, the synthetic drugs are not free from side effects which cause not only illnesses but also worsening them. One of the major side effects of synthetic drugs include resistance to the medicine. This is the turning point for the medicinal world to get back to the herbal medicine. Therefore, these circumstances compelled the researchers to shift their concentration to use herbal medicines instead of synthetic ones due to their less side effects, easily available and having productive results against several bacterial, fungal, leishmanial and other pathogenic infections.

Key words: Diseases; Herbs, Herbal therapy; Medicine; Resistance

INTRODUCTION

Since ancient times plants derivatives are being used as drugs as well as nutritional supplements by human beings. Almost half of the existing pharmaceutical kinds of stuff evolved from plants but they were not tested as antimicrobials. Secondary metabolites like alkaloids, flavonoids, terpenoids and tannins having in vitro antimicrobial activities are main components of plants [1]. They are being used by plants as shielding molecules and are responsible for their biological effects. Due to their great importance in the health-care system, plants are highly effective for human beings. Even raw materials of plants are useful for certain disorders and new compounds can be explored with the help of their chemical structures [2]. Nowadays, medicinal plants have gained huge importance due to their unique attributes of curative phytochemicals, which may lead to

the production of effective drugs. Many phytochemicals originated from plant sources like flavonoids and phenolics have optimistic influences on human health and prevention of cancer [3]. Conservative drugs and synthetic products are replaced by using attractive natural sources for production and expansion of skin products, which donated much in producing interest for pharmaceutical research and applications on commercial levels of medicinal plants [4]. Medicinal plants have excess amount of flavonoids and phenolic contents, with their antioxidant activities, can play a role in the inhibition of age-related disorders, specifically those caused by oxidative stress [5]. These are plants and plants derivatives, which fulfill the nutritional needs and provide various supplements for health care to the immense population of the world. Extracts from various plants are useful supplements for pharmaceutical productions, as plants are cheap and easily available sources for health care. The natural products gained from these sources are very beneficial with very fewer side effects and are being in practice since human history. Different communities have used different plants and plants extracts for various treatments. In certain nations, the utilization of restorative plants is regularly connected with black magic and superstition, since individuals do not have the logical understanding to clarify and anticipate the remedial activity of plants. However, with the passage of time, the use of these medicinal plants enhanced in emerging and developed nations as they have fewer side effects, low in cost and are naturally available but we may also grow them according to our needs [6]. Generally, in the emerging world, individuals have less access to present-day drugs and in this way, they consume distinctive conventional herbal inventions to combat illnesses [7]. There are 350 traditional herbal remedies in Pakistan, used to cure several ailments [8]. Medicinal plants that provide a possible linkage to the therapeutic activities of medicines are rich in various essential contents. Plants have the capability of high intake of various essential contents from the soil in response to concentration gradients [9]. Research has demonstrated that due to the non-biodegradable nature of components, they have a tendency to mount up in the biological compartment and travel through the food chain, producing an influence on general body functions [10]. Many

countries in Asia are busy in developing, strengthening and introducing the use of traditional medicine into primary healthcare [11, 12]. The herbal medicines together with herbal products, herbal preparations and raw herbs are utmost widespread use of conventional drugs [13]. Herbal medicines are frequently used by the women [14, 15]. They use these herbal medicines for the treatment of various ailments like regulating the menstrual cycle, abortifacients, fertility, menopause, postpartum and labor aids [16, 17]. Nature has given the treatment for every disease in natural resources, now it depends on human being to find them and make use of them. Since long both humans and livestock use these natural resources as potential drugs, and these natural medicines are further processed to make useful drugs each especially for a specific disorder [18]. Around 400,000 of plant species are being reported throughout the globe and only between 1-10% are used as food by humans and other animals [19]. The conventional drugs play a vital role in people's lives in emerging countries where more than one-third of the population do not have access to necessary medicines and these herbal remedies have long been utilized with the great contributions made by the primary healthcare facilitators at the community level [20]. When it comes to females' healthcare specifically that are utilized in pregnancy and postnatal period, a lot of communities have unique practices regarding these herbal therapies [21, 22]. In most of the communities, puerperium, pregnancy and childbirth are the critical periods in their lives [23]. As per the world health organization (WHO) reports, 80% of human beings in under-developed countries are dependent on these herbal medicines for their primary health care system. Nowadays, a huge amount of pharmaceutics used for the health care system is actually of plants origin inspired by their traditional use [24].

There are many objectives of utilizing plants like; a source of healing agents, to separate bioactive components used in drugs, to prepare bioactive components of innovative structures, to utilize agents as pharmacologic instruments and to use the entire plant or part of it as a herbal medication [25]. Considerably, plants produce chemicals like primary and secondary metabolites which have important applications in present day treatment. Modern allopathic

medicines have their roots in prehistoric medication and it is certain that numerous other important medications will be revealed and commercialized in near future.

Discovery of medicines from therapeutic plants has conventionally been lengthier and more complex than other methods of medicinal discoveries. In this way, numerous pharmaceutical companies have reduced their research on natural products [26]. However, in recent times there has been a restoration of concentration in reviving natural products, as indicated by one authority "We would not have the top-selling drug class today, the statins; the whole field of angiotensin antagonists and angiotensin-converting enzyme inhibitors; the whole area of immunosuppressive, nor most of the anticancer and antibacterial drugs. Imagine all of these drugs not being available to physicians or patients today". Obviously, nature has played and will keep on playing a vital role in the process of drugs discovery [27]. Pharmaceuticals and mainstream researchers have recently gotten the consideration of the therapeutic plants and different publications have acknowledged the therapeutic value of natural compounds to certify the claims of their biological actions. Abundant use of commercially available antibiotics and other synthetic pesticides for humans and agriculture purposes are harmful to our health, ecosystem and environment. Similarly, consideration has been drawn to the antimicrobial properties of plants and their metabolites because of their growth rates of drug-resistant pathogens of both medical and agriculture significance. Therapeutic plants have an inborn capability to oppose pathogenic microorganisms and this has directed the researchers to examine their mechanism of action and to isolate their active compounds. This has empowered taking advantage of medicinal plants for the treatment of microbial infections of humans as well as plants by developing novel antimicrobial agents [28]. In perspective of the vast numbers of the plant species possibly accessible for the study, it is necessary to have effective systems of methods to appraise the efficiency of medicinal plants as anti-microbial agents. The appraisal for antimicrobial agents of plants initiates with thorough and systematic biological evaluation of plant extracts to make sure effectiveness and safety

pursued by identification of dynamic principles and dosage formulation of new drugs [29].

ANTIBACTERIAL ACTIVITY

Anything, which can terminate bacteria or oppresses their growth or their capability to replicate are antibacterial in nature and their mode of action is known as antibacterial activity. Heat and chemicals, for example, chlorine and antibiotic drugs all have antibacterial properties [30]. Thus, anti-bacterial activity is known as the activity by which the growth of bacteria is smashed or repressed. It is likewise defined as the function of surface area in interaction with the microorganisms [31]. Although anti-bacterial agents are selective concentration remedies, proficient of damaging or inhibiting the growth of bacteria and they are friendly to their hosts. These compounds perform as chemotherapeutic operators for the treatment or anticipation of bacterial disorders. An anti-bacterial agent is considered as the agent, which kills bacteria, or as bacteriostatic if it prevents their growth and development [32]. Recently, interest has been developed in investigating and evolving new anti-bacterial agents from different sources to overcome the problem of bacterial resistance. For that reason, more attention is being paid to anti-bacterial actions screening and appraising techniques [33]. Anti-biotic drugs resistance has to turn into a serious and extensive issue in emerging countries cause high mortality every year [34]. Inappropriate use of anti-biotic agents is the utmost effective factor of antibiotic resistance. In addition, the worldwide appearance of multidrug resistant bacteria gradually restrains the efficiency of existing drugs and noticeably bring about treatment failure [35]. Anti-biotic resistance resulting in reduced efficiency of anti-bacterial drugs, therefore, making the patient's treatment very challenging, expensive or sometimes impossible. Anti-biotic resistance is hard to lessen, however, one tactic to evade this is by consuming alternative medicinal agents from plants, which are more effective against anti-biotic resistant bacteria, harmless, easily available and are low in cost [36]. The bacterial infections are still amongst the major causes of illnesses and mortality throughout the globe, the circumstances are

becoming more complex by the appearance and development of multi drugs resistant strains [37]. These days, bacterial infections are amongst the most important infectious disorders. Therefore, more than 50 years of wide-ranging scientific studies have been propelled for attaining new anti-microbial medications isolated from various sources. Despite the extensive improvement in the development of anti-bacterial mediators, there are very special necessities to discover new anti-bacterial agents, due to the development of multidrug-resistant bacteria [38]. Thus with the appearance of pathogenic bacterial strains, that have an opposition towards a number of antibiotics, the medicinal world requires new classes of dis-infection systems [39]. For this purpose, extracts of some plants are being examined. *Achillea santolina* applied anti-microbial activity in contradiction of *Candida albicans, Pseudomonas aeruginosa* and *Staphylococcus aureus.* MICs (Minimum Inhibitory Concentrations) of *Achillea santolina* extracts against this microorganism were 40, 60 and 12 ppm respectively. Noticeable anti-bacterial activity against *a-hemolytic Streptococci* and *Staphylococcus aureus* has been informed for *Agrimonia eupatoria.* Methanolic extracts from leaves and hydrodistilled residues of *Ailanthus altissima* were efficient against gram-positive bacteria. The essential oil extracted from the seeds of *Anethum graveolens* and their various other extracts employed anti-microbial activity against wide-range of microorganisms [40]. However, many other plants are under study, while the rest of the plants need to be examined for their biological activities.

ANTIFUNGAL ACTIVITY

Pathogenic fungi are the leading infectious agents in plants population, triggering alterations throughout developmental stages comprising post-harvest. In vegetables and fruits, there are comprehensive variability of fungal genera, causing quality issues related to aspect, organoleptic characteristics, nutritional value and limited shelf life [41]. In some other cases, fungi are indirectly accountable for allergic or toxic ailments between consumers because of the production of allergens or mycotoxins [42]. Normally, phytopathogenic fungi are controlled with the help of synthetic

fungicides, however, their usage is increasingly limited due to the harmful side effects of pesticides on both human health and environment [43]. Fungi are everywhere in the environment and the infections due to fungal-pathogens have turned into more common ones. The genus: *Alternaria needs* are the most widely distributed fungi in nature and their species are amongst the most common one on the phyllo-sphere. They include both plant-saprophytic and plant-pathogenic species, which may damage the crops in fields or cause post-harvest decay, bringing about the considerable economic loss for the farmers and to food industries [44]. Fungal infections pose serious and continuous threats to human well-being and life. In human, the infections caused by these fungal agents are separated into the following classes (i) toxic reactions to toxins existing in certain fungi, (ii) infections (mycoses) and (iii) fungal-proteins allergic reactions. Healthy people are vulnerable to the host of cutaneous, sub-cutaneous, superficial and in some cases integral infections which may originate various circumstances extending from infections of nail's, athlete's foot to dispersed diseases such as *Histoplasmosis*. Among these fungal infections, numerous fungal infections mainly induce due to adaptable pathogens which may be endogenous like infections of *Candida* or attained from the surroundings such as infections of *Aspergillus* and *Cryptococcus* [45]. Some other kinds of fungal infections that are aggressive and dermatomycoses developed by fungal creatures in those people which are highly vulnerable such as patients of cancer receiving chemo-therapy, neonates, burns patients, patients of organ transplant and besides them, those suffering from the fatal disease of AIDS. Corticosteroid and antibiotic treatments, lesions of epidermis and dermis, surgery, diabetes, malnutrition and neutropenia are among the other risk factors [46]. *Aspergillus* and *Candida* spp. are responsible for most of the familiar infections. Recent epidemiological patterns demonstrate a swing in the direction of infections due to *Aspergillus* spp., a non-albicans, *Candida* spp. and formerly unusual fungi that frequently reduced the vulnerability to current anti-fungal agents [47]. Clinically, aspergillosis and candidiasis represent somewhere in the range of 80% to 90% of systemic fungal infections in immune-compromised patients [48]. There are significant cautions among the medicinal

profession on the subject of fungal diseases. Dermatophyte infections like candidiasis and tinea pedis even though rarely fatal, are commonly widespread all over the globe. Pathogens such as *Aspergillus fumigatus, Cryptococcus neoformans, Candida albicans* and *Pneumocystis carinii* are the important factors in immuno-compromised patients responsible for significant amount of morbidity and mortality [49]. Over the past three decades, the occurrence of systemic fungal infections has dramatically increased due to an increase in the number of immune-compromised hosts. Even though the arsenal of anti-fungal drugs has prolonged, currently available anti-fungal drugs are helpless to meet the expanding prerequisites to deal with the infection in a complicated patient's community. Thus, the production of novel anti-fungal agents are continuously needed in medicinal therapeutics [50].

ANTILEISHMANIAL ACTIVITY

The infection caused by protozoa of the genus; *Leishmania,* is the major health issue worldwide, having extraordinary endemicity in emerging countries. Leishmaniasis is considered as the major health issue of a community [51], causing noteworthy morbidity and mortality in various countries of Asia, Africa and Latin America. About 350 million people including children in 88 countries around the world are suffering from this disease, of which around 2 million people affected per annum. This rapid increase in the rate of leishmaniasis may be associated with urbanization, the devastation of forests, changes in the environment and the migration of people to those areas where this infectious disease is endemic [52]. Human leishmaniasis is caused due to the species of the genus; *Leishmania* a protozoan, member of the hemo-flagellate group, which has their reservoir in rodents, dogs, penguins, marsupials and many other wild animals which is transmitted by the bite of mosquitoes belonging to the genera; *Lutzomia* and *Phlebotomus.* The term leishmaniasis contains three distinctive clinical manifestations i-e., cutaneous leishmaniasis, generalized visceral infection and mucocutaneous leishmaniasis [53]. There are many difficulties in the way of treatment for leishmaniasis due to the intra-macrophagic position of

the infectious form. The patients of this disease are immuno-deficient thus, are unable to remove the parasite through a normal body own defense mechanism. Furthermore, malnutrition is also linked with several cases of leishmaniasis. The infection in parallel with other diseases like malaria and pneumonia enhances the fatalness of the infection if it is not diagnosed and treated within time. The leishmanial problem has been aggravated by the evolution of AIDS because of parallel infection in AIDS patients and as well as by the development of drugs-resistance by parasites [54]. Without a suitable vaccine, there is a need for operative drugs on an urgent basis to replace currently used medicines. The drugs clinically utilized for this purpose were produced before 1959, most of which are centered on pentavalent antimony compounds. The toxicity level of these mediators and the perseverance of side effects even after modification of the dosage level and period of treatment are however extreme downsides. There are many complexions in the way to search for anti-leishmanial agents. The usage of alternative drugs like *pentamidine* and *amphotericin-B* also have worse side effects [55]. Whereas, plant extracts and their derivatives possibly provide a valuable source of new medicinal drugs [56] and the serious need for alternative treatment has led the researchers to a program of screening natural kinds of stuff for potential use in therapy of leishmanial infections. In fact, WHO advocated the use of traditional herbal therapy in areas where suitable health care services are unapproachable [57]. Generally, leishmaniasis treatment efficiency depends on various factors including the type of drug, immune response of the host, strain of parasite and the way of treatment. Thus, the search for developing new chemical agents is ongoing that show low toxicity, highly active and low in cost. According to scientific studies, medicinal plants have very exciting characteristics for the production of new leishmanicidal drugs. These natural products also have several biological functions in response to various pathogens and are abundantly available in nature [58]. The researchers have claimed that more than 90% cases of visceral leishmaniasis happens in India, Bangladesh, Brazil, Nepal, South Sudan and Ethiopia whereas, around 75% cases of cutaneous leishmaniasis happen generally in Algeria, Afghanistan, Brazil, Costa Rica, Colombia Ethiopia, Iran, North Sudan, Peru and Syria [59].

CONCLUSION

From this review, it is concluded that the use of medicinal plants and their extracts got importance in the daily life of human beings as they have the ability to fulfill the nutritional needs as well as provide medicinal therapy. Consequently, they produce many extracellular and intracellular metabolites which carry enormous biotechnological applications. Almost all classes and groups of plants produce bioactive compounds of different characteristics. These plant metabolites carry antibacterial, antifungal, anti-cancerous, anti-leishmanial and antioxidant potentials. Nevertheless, the health hazards and environmental concerns of synthetic medicine compel researchers to work and find substitute of such synthetic medicine. To overcome this problem, new components are to be sought that show good outcomes against these infectious agents.

REFERENCES

1. Rampadarath S, Puchooa D & Ranghoo-Sanmukhiya VM (2014). A comparison of polyphenolic content, antioxidant activity and insecticidal properties of Jatropha species and wild Ricinus communis L. found in Mauritius. *Asian Pacific journal of tropical medicine*, *7*, S384-S390.
2. Tasleem F, Azhar I, Ali SN, Perveen S & Mahmood ZA (2014). Analgesic and anti-inflammatory activities of Piper nigrum L. *Asian Pacific journal of tropical medicine*, *7*, S461-S468.
3. Azwanida NN (2015). A review on the extraction methods use in medicinal plants, principle, strength and limitation. *Med. Aromat. Plants*, *4*(3), 3-8.
4. Mukherjee PK, Maity N, Nema NK & Sarkar BK (2011). Bioactive compounds from natural resources against skin aging. *Phytomedicine*, *19*(1), 64-73.
5. Azwanida NN (2015). A review on the extraction methods use in medicinal plants, principle, strength and limitation. *Med. Aromat. Plants*, *4*(3), 3-8.

6. Basu S, Das M, Sen A, Choudhury UR & Datta G (2014). Analysis of complete nutritional profile and identification of bioactive components present in Alocasia indica tuber cultivated in Howrah District of West Bengal, India. *Asian Pacific journal of tropical medicine*, *7*, S527-S533.
7. Calixto JB (2005). Twenty-five years of research on medicinal plants in Latin America: a personal view. *Journal of ethnopharmacology*, *100*(1-2), 131-134.
8. Ahmad SS & Husain SZ (2008). Ethno medicinal survey of plants from salt range (Kallar Kahar) of Pakistan. *Pak. J. Bot*, *40*(3), 1005-1011.
9. Aziz MA, Adnan M, Begum S, Azizullah A, Nazir R & Iram S (2016). A review on the elemental contents of Pakistani medicinal plants: Implications for folk medicines. *Journal of ethnopharmacology*, *188*, 177-192.
10. Živković J, Ražić S, Arsenijević J & Maksimović Z (2012). Heavy metal contents in Veronica species and soil from mountain areas in Serbia. *Journal of the Serbian Chemical Society*, *77*(7), 959-970.
11. Shein K 2001. Traditional Medicine in Asia, SEARO Regional Publications (no.39), World Health Organization Regional Office for south east Asia, New Delhi, India.
12. WHO 2004. Guidelines on Safety Monitoring of Herbal Medicines in Pharmacovigilance Systems. WHO, Geneva.
13. WHO 2008. Traditional medicine [WWWDocument]. World Health Organization. URL: (http://www.who.int/mediacentre/factsheets/fs134/en/indes.html)
14. Murphy PA, Kronenberg F & Wade C (1999). Complementary and alternative medicine in women's health: developing a research agenda. *Journal of Nurse-Midwifery*, *44*(3), 192-204.
15. Hall HG, Griffiths DL & McKenna LG (2011). The use of complementary and alternative medicine by pregnant women: a literature review. *Midwifery*, *27*(6), 817-824.
16. Beal MW (1998). Women's use of complementary and alternative therapies in reproductive health care. *Journal of nurse-midwifery*, *43*(3), 224-234.

17. Shukla R, Chakravarty M & Gautam MP (2008). Indigenous medicine used for treatment of gynecological disorders by tribal of chhattisgarh, India. *Journal of Medicinal Plants Research*, *2*(12), 356-360.
18. Chmit M, Kanaan H, Habib J, Abbass M, Mcheik A & Chokr A (2014). Antibacterial and antibiofilm activities of polysaccharides, essential oil, and fatty oil extracted from Laurus nobilis growing in Lebanon. *Asian Pacific journal of tropical medicine*, *7*, S546-S552.
19. Cowan MM (1999). Plant products as antimicrobial agents. *Clinical microbiology reviews*, *12*(4), 564-582.
20. De Wet H & Ngubane SC (2014). Traditional herbal remedies used by women in a rural community in northern Maputaland (South Africa) for the treatment of gynaecology and obstetric complaints. *South African Journal of Botany*, *94*, 129-139.
21. Mathews M & Manderson L (1981). Vietnamese behavioral and dietary precautions during confinement. *Ecology of Food and Nutrition*, *11*(1), 9-16.
22. Jambunathan J & Stewart S (1995). Hmong women in Wisconsin: What are their concerns in pregnancy and childbirth?. *Birth*, *22*(4), 204-210.
23. LE MINH THI (2004). *Traditional Postpartum Practices Among Vietnamese Mothers: A Study in Anthi District, Hungyen Province* (Doctoral dissertation, Mahidol University).
24. Aziz MA, Khan AH, Adnan M & Izatullah I (2017). Traditional uses of medicinal plants reported by the indigenous communities and local herbal practitioners of Bajaur Agency, Federally Administrated Tribal Areas, Pakistan. *Journal of ethnopharmacology*, *198*, 268-281.
25. Fabricant DS & Farnsworth NR (2001). The value of plants used in traditional medicine for drug discovery. *Environmental health perspectives*, *109*(Suppl 1), 69.
26. Butler MS (2004). The role of natural product chemistry in drug discovery. *Journal of natural products*, *67*(12), 2141-2153.

27. Cragg GM & Newman DJ (2005). Biodiversity: A continuing source of novel drug leads. *Pure and applied chemistry*, *77*(1), 7-24.
28. Das K, Tiwari RKS & Shrivastava DK (2010). Techniques for evaluation of medicinal plant products as antimicrobial agents: current methods and future trends. *Journal of medicinal plants research*, *4*(2), 104-111.
29. Tanaka JCA, Da Silva CC, De Oliveira AJB, Nakamura CV & Dias Filho BP (2006). Antibacterial activity of indole alkaloids from Aspidosperma ramiflorum. *Brazilian Journal of Medical and Biological Research*, *39*(3), 387-391.
30. https://www.medicinenet.com/script/main/art.asp?articlekey=10215
31. Wahab R, Kim YS, Mishra A, Yun SI & Shin HS (2010). Formation of ZnO micro-flowers prepared via solution process and their antibacterial activity. *Nanoscale research letters*, *5*(10), 1675.
32. Sirelkhatim A, Mahmud S, Seeni A, Kaus NHM, Ann LC, Bakhori SKM & Mohamad D (2015). Review on zinc oxide nanoparticles: antibacterial activity and toxicity mechanism. *Nano-Micro Letters*, *7*(3), 219-242.
33. Balouiri M, Sadiki M & Ibnsouda SK (2016). Methods for in vitro evaluating antimicrobial activity: A review. *Journal of pharmaceutical analysis*, *6*(2), 71-79.
34. Gyles C (2011). The growing problem of antimicrobial resistance. *The Canadian Veterinary Journal*, *52*(8), 817.
35. Djeussi DE, Noumedem JA, Seukep JA, Fankam AG, Voukeng IK, Tankeo SB & Kuete V (2013). Antibacterial activities of selected edible plants extracts against multidrug-resistant Gram-negative bacteria. *BMC complementary and alternative medicine*, *13*(1), 164.
36. Wikaningtyas P & Sukandar EY (2016). The antibacterial activity of selected plants towards resistant bacteria isolated from clinical specimens. *Asian Pacific Journal of Tropical Biomedicine*, *6*(1), 16-19.
37. Dzotam JK, Touani FK & Kuete V (2016). Antibacterial activities of the methanol extracts of Canarium schweinfurthii

and four other Cameroonian dietary plants against multi-drug resistant Gram-negative bacteria. *Saudi journal of biological sciences*, *23*(5), 565-570.

38. Wise R, Hart T, Cars O, Streulens M, Helmuth R, Huovinen P & Sprenger M (1998). Antimicrobial resistance.
39. Le Ouay B & Stellacci F (2015). Antibacterial activity of silver nanoparticles: a surface science insight. *Nano today*, *10*(3), 339-354.
40. Al-Snafi AE (2015). Therapeutic properties of medicinal plants: a review of their antibacterial activity (part 1). *International Journal of Pharmacology and Toxicology*, *6*(3), 137-158.
41. Agrios GN (2004). Losses caused by plant diseases. *Plant Pathology. Elsevier, Oxford, UK*, 29-45.
42. Dellavalle PD, Cabrera A, Alem D, Larrañaga P, Ferreira F & Dalla Rizza M (2011). Antifungal activity of medicinal plant extracts against phytopathogenic fungus Alternaria spp. *Chilean Journal of Agricultural Research*, *71*(2), 231.
43. Harris CA, Renfrew MJ & Woolridge MW (2001). Assessing the risks of pesticide residues to consumers: recent and future developments. *Food Additives & Contaminants*, *18*(12), 1124-1129.
44. Lopes MC & Martins VC (2008). Fungal plant pathogens in Portugal: Alternaria dauci. *Revista Iberoamericana de Micología*, *25*(4), 254..0
45. Kathiravan MK, Salake AB, Chothe AS, Dudhe PB, Watode RP, Mukta MS & Gadhwe S (2012). The biology and chemistry of antifungal agents: a review. *Bioorganic & medicinal chemistry*, *20*(19), 5678-5698.
46. Lv Z, Sheng C, Zhang Y, Wang T, Feng J, Sun H & Li K (2010). Synthesis and in vitro antifungal activities of new 3-substituted benzopyrone derivatives. *Bioorganic & medicinal chemistry letters*, *20*(23), 7106-7109.
47. Groll AH & Walsh TJ (2001). Uncommon opportunistic fungi: new nosocomial threats. *Clinical Microbiology and Infection*, *7*, 8-24.

48. Onnis V, De Logu A, Cocco MT, Fadda R, Meleddu R & Congiu C (2009). 2-Acylhydrazino-5-arylpyrrole derivatives: synthesis and antifungal activity evaluation. *European journal of medicinal chemistry*, *44*(3), 1288-1295.
49. Salaün J (2000). Cyclopropane derivatives and their diverse biological activities. In *Small ring compounds in organic synthesis VI* (pp. 1-67). Springer, Berlin, Heidelberg.
50. Tang H, Zheng C, Lv J, Wu J, Li Y, Yang H & Zhu J (2010). Synthesis and antifungal activities in vitro of novel pyrazino [2, 1-a] isoquinolin derivatives. *Bioorganic & medicinal chemistry letters*, *20*(3), 979-982.\
51. World Health Organization (WHO) 2002. Programme for the surveillance and control of leishmaniasis (http://www.who. int/emc/diseases/leish/index.html). Accessed 04/02/2002.
52. Rocha LG, Almeida JRGS, Macedo RO & Barbosa-Filho JM (2005). A review of natural products with antileishmanial activity. *Phytomedicine*, *12*(6-7), 514-535.
53. Ashford RW (2000). The leishmaniases as emerging and reemerging zoonoses. *International journal for parasitology*, *30*(12-13), 1269-1281.
54. De Carvalho PB, Arribas MDG & Ferreira EI (2000). Leishmaniasis. What do we know about its chemotherapy?. *Revista Brasileira de Ciências Farmacêuticas*, *36*(1), 69-96.
55. Balaña-Fouce R, Reguera RM, Cubrıa JC & Ordóñez D (1998). The pharmacology of leishmaniasis. *General Pharmacology: The Vascular System*, *30*(4), 435-443.
56. Kayser O & Kiderlen AF (2001). In vitro leishmanicidal activity of naturally occurring chalcones. *Phytotherapy Research*, *15*(2), 148-152.
57. Weniger B, Robledo S, Arango GJ, Deharo E, Aragón R, Muñoz V & Anton R (2001). Antiprotozoal activities of Colombian plants. *Journal of ethnopharmacology*, *78*(2-3), 193-200.
58. Da Silva BJM, Hage AAP, Silva EO & Rodrigues APD (2018). Medicinal plants from the Brazilian Amazonian region and

their antileishmanial activity: a review. *Journal of integrative medicine*.

59. Sangshetti JN, Khan FAK, Kulkarni AA, Arote R & Patil RH (2015). Antileishmanial drug discovery: comprehensive review of the last 10 years. *Rsc Advances*, *5*(41), 32376-32415.