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Original Research Article

Plants as a source of a novel anti-typhoid therapeutic agents: A Review

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Abstract

Typhoid fever is now becoming the deadly danger disease day by day because of the resistance power developed by Salmonella typhi, Salmonella paratyphi A, Salmonella paratyphi B; which cause typhoid fever, paratyphoid A and B fevers respectively. This situation has created a need to find more effective drugs. Natural products from microorganisms have been the primary source of antibiotics, and with the increasing acceptance of herbal medicines, the screening of medicinal plants for new active compounds has become a very important source of novel antibiotics. Alternative herbal medicine has been used to treat various infections from centuries. Natural plants contain phytoconstituents having similar chemical properties as of synthetic antibiotics. In future plants may be the source of effective treatments against typhoid and many more diseases.

Key Words: Typhoid, Medicinal plants, Herbal drugs, Anti-typhoid drugs.

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INTRODUCTION

Typhoid fever, which is caused by Salmonella enterica serovar Typhi, remains a major public health threat in developing countries. Approximately 13.5 million cases occur annually, and the disease was associated with 190 000 deaths worldwide in 2010.[1,3] In developed areas, such as Europe and North America, the incidence of typhoid fever is very low, whereas in many developing countries, such as Africa, Latin America and South or Southeast Asia, the disease is endemic. For example, the annual incidence of typhoid fever has been as high as 573 cases per 100 000 individuals in Indonesia.[1,2]. Typhoid is a systemic disease characterized by fever and abdominal pain caused by dissemination of *S. typhi* or *S. paratyphi*. The major route of entry in humans bloodstream and intestinal tract through *S. typhi* or *S. paratyphi* infected foods or drinking water(S) Salmonella is one of the genera of the Enterobacteriaceae family. Among the Salmonellae of medical importance are *Salmonella typhi*, *Salmonella paratyphi A*, *Salmonella paratyphi B*; which cause typhoid fever, paratyphoid A and B fevers respectively[4]. *Salmonella typhimurium* is the species responsible for typhoid fever in animal experimental models. Enteric fever remains an important public health problem in developing countries. There are approximately 22 million typhoid cases and 2,16,510 deaths occur per year globally with majority of cases occurring in Asia, especially in the Indian subcontinent[5,6]. The disease is an invasive infection commonly caused by *Salmonella enterica* serovars Typhi and Paratyphi A. Enteric fever is endemic in many developing countries, including India and, if not treated appropriately, has a mortality rate of 30%. Appropriate treatment reduces the mortality rate to as low as 0.5%[7]. The common treatment options used for enteric fever are ciprofloxacin, ceftriaxone and cefixime[8]. It is also suggested that the specific treatment of enteric fever used to be chloramphenicol, trimethoprim-sulfamethoxazole or ampicillin and also found that the causative organism, *Salmonella enterica* serovar Typhi (*S.* Typhi) has rapidly gained resistance to these

antibiotics[9,10] Now the currently used drugs against *S. Typhi* is fluoroquinolones, such as ciprofloxacin, became the drug of choice for the treatment of enteric fever[11]. This situation has created a need to find more effective drugs. Natural products from microorganisms have been the primary source of antibiotics, and with the increasing acceptance of herbal medicines, the screening of medicinal plants for new active compounds has become a very important source of novel antibiotics[4].Presently there are a great number of antibiotics available to treat microbial infections, however it has also been noticed that many infectious agents have attained resistance to several of these antibiotics. The countries in the region such as Malaysia, Indonesia, Brunei, and Thailand have a long history of using medicinal plant that proffers substantial pharmaceutical prospects[12]. Ayurveda, the Indian system of natural medicine has been practiced for over two thousand years[13,14]. The response of certain types of infections to antibiotics is poor. Ayurvedic formulations are usually prepared from root, stem, leaf, flower and fruits of medicinal plants. Various infections caused by bacteria, fungi, virus, parasite as well non-infectious metabolic disorders are effectively treated with herbal/Ayurvedic formulations[15] *Paullinia pinnata Linn* (Sapindaceae) is a medicinal plant, locally used in the West Region of Cameroon for the treatment of typhoid fever. This work was designed to evaluate the antityphoid and antioxidant activities of the extracts and compounds of *P. pinnata*. Ethanolic extract of *propolis* was used to check the antibacterial potential of propolis in combination with the standard antibiotic Cefixime against the typhoid causing bacteria i.e. Salmonella and it was found that the *Propolis* acted synergistically with cefixime and enhanced the efficacy of antibiotic and reduced its effective dose in combined therapy.[16] *Harungana madagascariensis L* is commonly used in Cameroonian folk medicine for the treatment of malaria and typhoid fever. The *in vivo* anti salmonellae study[17] was carried out and found that *H. madagascariensis* has a promising anti-salmonellae effect and, therefore, the potential to provide an effective treatment against salmonellosis, including typhoid fever. Commonly used medicinal plants and vegetables not only posses the essential nutrients but also reported to contain secondary metabolites such as; alkaloids, flavonoids, glycosides, terpenoids and phenolics[18,19]. *Glycyrrhiza glabra and Azadirachta indica* both plants extract is effective against salmonella typhi[19] The *liquorice and neem* both are used as a traditional medicine all over the world. Methanol extracts of plant parts commonly used in Cameroon for the treatment of typhoid fever were tested for antibacterial activity against *Salmonella typhi, S. paratyphi and S. typhimurium*. The formulations used were: 1) Formulation A comprising *Cymbogogon citratus* leaves, *Carica papaya* leaves, and *Zea mays* silk. 2) Formulation B comprising C. papaya roots, *Mangifera indica* leaves, Citrus limon fruit and C. citratus leaves. 3) C. papaya leaves. 4) Emilia coccinea whole plant. 5) Comelina bengalensis leaves. 6) *Telfaria occidentalis* leaves. 7) *Gossypium arboreum* whole plant. Antimicrobial activity was tested using the minimum inhibitory concentration (MIC) and the minimum bactericidal concentration (MBC) and concluded that, plant extracts with low MIC and MBC values (1 mg/ml and lower) may contain compounds with therapeutic activity.[20] Ethanol and hot water extracts of *V. doniana* (Root extract) and *A. boonei* (bark) had the best anti-typhoid activity in the Ebonyi state, Nigeria[21] These plants were screened in-vitro for anti-typhoid activity against 10 clinically selected isolates of *S. typhi* using the hole-plate diffusion method. The Minimum inhibitory concentration (MIC) of Ethanol, hot and cold water extract of each herbal plant was determined by broth dilution method. According to the survey carried out in 2011[22] in the the Wa Municipality and Wa East (Funsi) District of the Upper West Region of Ghana found that Twenty-one species from ten families were cited for the treatment of typhoid fever. All of the above mentioned review articles strongly suggested that the different parts of the plants have the potential to cure microbial infections and availed us the opportunity to produce the ayurvedic drugs. In all, 38 plants were searched as an anti typhoid and thus these plants must have possesses the anti typhoid compound/s. All the above mentioned article was tested the anti-typhoid potential of plants using the minimum inhibitory concentration (MIC) and the minimum bactericidal concentration (MBC). Few of the above mentioned articles isolated, characterized and identified the Plant compound/s responsible for the inhibition of growth for the *S. typhi* and *S. paratyphi*

MATERIALS AND METHODOLOGY

Research articles on antityphoid, typhoid therapeutic drugs and medicinal plants published in journals, books, and reports were reviewed. Relevant literatures were searched in Google Scholar and various electronic databases including NCBI PUBMED, Science Direct, IEEE Xplore, Scopus, SciFinder, and MEDLINE using a specific search terms including “anityphoid”, “medicinal plants”, “Typhoid”, “Typhoid India and therapeutic drugs.

Collection of bacteria strains: In the above mentioned research articles the clinical isolates of *S. typhi and S. paratyphi* were isolated from patients and all Isolates was identified and characterized using standard microbiology technique[23].

Sources of plants and Preparation of plant extracts: All plant materials were collected, identified and voucher specimen were kept in the herbarium for the further use during the experiment. Different part/parts of each medicinal plant/s were collected and properly washed and rinsed in sterile distilled water. It was allowed to dry under room temperature, pulverized using laboratory mortar and pestle and further with manual hand grinding machine and was stored in air tight containers for further analysis.

Extraction of plant materials: Plant materials were extracted with the different solvents like methanol, ethanol, cold and hot water, Each preparation was filtered using Whattman No 1 filter paper and was evaporated to dryness in a steady air current for 24 h in a previously weighed crucible.

Determination of anti-typhoid activity (*In vivo* therapeutic test and In-vitro): The different solvent extracts of each herbal plant was spot checked for anti-typhoid activity using the agar well diffusion method[24]. After incubation the radial zones of inhibition was measured around each of the extract. Ciprofloxacin and chloramphenicol mainly was used as control antibiotics.

Ethical guidelines: The In vivo therapeutic test was conducted according to the ethical guidelines of Committee for Control and Supervision of Experiments on Animals, Government of India, on the use of animals for scientific research. The crude extract was used in the treatment of infected animals. Mostly *Salmonella typhimurium*-induced typhoid model in Whistar rat is used as an experimental model animal[15]

RESULTS

This review article was focused on the medicinal plants with respect to anti-typhoid compounds And the causative agents of typhoid its current status and the available treatments for typhoid. The common treatment options used for enteric fever are ciprofloxacin, ceftriaxone and cefixime[8] Now the currently used drugs against *S.* Typhi is fluoroquinolones, such as ciprofloxacin, became the drug of choice for the treatment of enteric fever[11]. 26 research articles was reviewed and found that plants from the different regions of the world have the anti-typhoid potential. Very few research articles[25,15] identified the anti-typhoid compounds from the different part/s of the plant/s whereas other researchers only showed the anti-typhoid activity of medicinal plants on the basis of zone of inhibition against the causative organisms mentioned above and some of them also illustrates the In vivo therapeutic potentiality of crude extracts of plants on experimental animals like Whistar rat[15]. Total 38 plants from different families and different geographical regin was found to have antityphoid potentiality.

CONCLUSION

Typhoid fever, which is caused by Salmonella enterica serovar Typhi, remains a major public health threat in developing countries. The common treatment options used for enteric fever are ciprofloxacin, ceftriaxone and cefixime[8]. Vaccination is also the treatment for the typhoid. Considering the side effects of the allopathic drugs on human health, its necessary to develop the alternate route to develop the drugs from plants. This review article very clearly explain the methods used by researchers in order to develop the Ayurvedic drugs like agar well diffusion, micro broth dilution, extraction of plants compounds, purification of crude extracts and In vivo therapeutic plants extract activity using experimental animals.

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