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A Review : Worldwide Medicinal Plants For Typhoid Fever

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ABSTRACT

Typhoid fever, an enteric disease caused by *Salmonella typhi*, plays an important role of global health matter, contributing to the economic encumbrance in most developed countries. Even more, antibiotic resistance has ensued in *Salmonella enterica*infection. These health problems have proposed a broad struggle towards more study for new source of antimicrobial products especially from medicinal plants due to more profitable. This study reviews medicinal plants related to the typhoid fever and their mechanisms of antimicrobial action. The investigation for this review were established via the databases PubMed, Google Scholar, online Science Direct, Science and Technology Index. Practically 26 medicinal plants from 23 families used for typhoid fever in worldwide countries were reported. Most of them are originated from African continent, Pakistan and India. Antisalmonella activity was mostly identified by in vitro (MIC and MBC). Generally, the chemical compounds contained in the plants are alkaloid, flavonoid, saponin, tannin, phenols, glycosides, steroid and terpenoid. Their mechanisms of actions are mediation of solute transport inhibition in membranes, affecting the phospholipid membranes of bacterial cell wall, inhibiting nucleic acid synthesis and inducing microbial cell membrane disruption. These results redound to the alternative and complementary medication of typhoid fever.

Keywords: *Typhoid Fever, Salmonella typhi, antimicrobial resistance, medicinal plants, complementary and alternative medicine.*

INTRODUCTION

Typhoid fever is a systemic illness caused by *Salmonella typhi*, which included in the Global Burden of Disease 2010[1]. Antibiotic resistance has occurred in Salmonella enterica infection, at first (1980s) to the classic first-line drugs from several different countries[2]. Since 20th century, transmission of *S.typhi* strains leading resistance to antimicrobials[3]. Previous study reported that multidrug-resistance (MDR) salmonella showed real evidence of hospital cost impact[4]. These health problems have encouraged a worldwide endeavor against more research for new provenience of antimicrobial materials especially from medicinal plants due to cheaper cost, higher activity and minimal side effects[5]. This article reviews medicinal plants related to the typhoid fever therapy and and mechanisms of action against S.typhi. The investigation for this review were established via the databases PubMed, Google Scholar, online Science Direct, Science and Technology Index. The document relevant analyzed and included in the study.

Medicinal plants are traditional medicine vitality, where approximately 44 percent of world population use them mostly in developed countries[6]. The utilization of medicinal plants in most developing countries as a primary effort for maintaining health has been considerably monitored by UNESCO[7]. In addition, an extension trust on the medicinal plants benefit in pharmacology industry has been expanded to the extraction and widely traded as drugs and chemotherapics[8].

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Several drugs frequently use medicinal plants to extract their active ingredients, like in case of antibiotics, laxatives, blood thinners and anti-malarial medications[9]. Presently, data on the antimicrobial activity of numerous plants, so far considered empirical, have been scientifically proved, with the increasing number of reports on pathogenic microorganisms resistant to antimicrobials. Active compounds derived from plants may potentially control microbial growth in various conditions and in the specific disease treatment[9]. Medicinal plants can make a significant endowment to WHO's programme by the year 2000, that all peoples, worldwide, will lead a sustainable socioeconomic productive life[10]. Trade in medicinal plants is evolving in capacity and in exports. In South Africa, likewise, some 500 species are commercialized trade products[10].

Typhoid fever is caused by Salmonella typhi and perennially be an evident public health issue in developing countries mainly in sub-Saharan Africa [11]. The ordinary antimicrobial drugs are becoming more unprepared to the population in Africa due to increased expenses[12]. Cases of resistance to the currently used antibiotics have been encountered with S.typhi, especially for the three first line antimicrobials (chloramphenicol, ampicillin and co-trimoxazole)[13]. Furthermore, chloramphenicol has been withdrawn from the trading due to its side effect in medullary toxicity [14].

MATERIALS AND METHOD

Nowadays, matching to the literature, many researchers concentrate on finding plant-derived medicines[10] and search for therapeutic agents from natural sources for the treatment of typhoid fevers[14] because medicinal plants had been reported to be safe and without side effect[15]. This review was conducted using systematic literature search on the worldwide medicinal plants for typhoid fever in the databases PubMed, Google Scholar, online ScienceDirect, Science and Technology Index, and Portal Garuda. The search keywords included "Salmonella typhi", "Salmonella typhi, typhoid fever and antimicrobial resistance", "Medicinal plants for typhoid fever", "anti-salmonella activity of plants" etc.

RESULTS AND DISCUSSION

Anti-Salmonella of Worldwide Medicinal Plants

Populations worldwide have used traditional medicine based on natural[16]. There is an enhancement utilize of herbal medicines globally with trust that they are always secure and without side effect because they are from natural ingredients[17].

Medicinal plants are mostly used in Africa, they are *Aloe trigonantha L.C. Leach, Crinum purpurascens, Paulliniapinnata Linn, Cleistropholis patens Benth, Emilia coccinea, Cymbogogoncitratus, Carica papaya, Zea mays, Telfariaoccidentalis, Cassia eucalyptus, Mangiferaindica, Morindalucida, Ocimumgratissimum, Anthocleistavogelii, Anthocleistadjalonensis and Cassia petersiana.*Leaf latex of *Aloe trigonantha L.C. Leach*contains aloesin and anthrone (structurally related to antraquinone), as well as *Cassia petersiana.* Previous study showed that the anthraquinones affect the phospholipid membranes of bacterial cell wall resulting in perturbations of the phospholipid membranes of bacterial cell wall[18]. Leaf extract of *Crinum purpurascens* comprisesâ-D -glucopyranoside of sitosterol which are active against *S.typhi* and *S.paratyphi B* and classified as bactericidal agents (ratio MBC/MIC $\leq$ 4)[14]. The methanol extracts of the leaves and stems of *Paulliniapinnata Linn*containing (3β)-3-O-(2′-Acetamido-2′-deoxy-β-D-glucopyranosyl) oleanolic acid, demonstrated antibacterial activities against *S.typhi*(MIC = 0.781-1.562 μg/ml) by inducing the proliferation of leucocyte and lymphocytes in the body[19]. Saponin fraction of stem bark extract of *Cleistropholis patens Benth*was active against S.typhi[20]. Composite of *C.citratus* leaves, *C. papaya* leaves, and *Zea mays* silk had inhibitory activity at 0.02 to 0.06 mg/ml while composite of *C.papaya* roots, *M.indica* leaves, *Citrus limon* fruit and *C. citratus* leaves had bacterial activity at 0.06 to 0.25 mg/ml[21,22].In Ivory Coast, the flowers of *Thonningiasanguinea* are used for the therapy of salmonellosis. Recent studies have shown inhibition of the multi drug resistant strain *Salmonella enteritidis*by the crude aqueous extract of *Thonningiasanguinea*. The secondary metabolites screening of the flowers extract of*Thonningiasanguinea* have shown the existence ofsaponins, quinons, polyphenols which are known to take possession of antibacterial activities[23]. Still from Africa, *Cassia eucalyptus*, which is revealed by the Nupes of Bida in Nigeria to be effective in typhoid fever medication, conceives alkaloid, tannin and saponin[24]. The study of *Telfairiaoccidentalis* indicated the presence of saponins, alkaloids, tannins, phenolics and denoted an antibacterial activity on *S.typhi* ((MIC and MBC

values of 5.0mgml)[21].*Mangiferaindica* (mango) leaves[25], *Camelia sinensis*[26], *Anthocleista vogeli*[27,28], *Anthocleista djalonensi*[27,29] , *Cassia petersiana*[30,31] , *Morinda lucida*[32], *Ocimum gratissinum*[32]have been reported for inhibitory effect against *S.typhi*. *C.petersiana*conceives alkaloids, flavonoids, cardiac glycosides, antraquinones, anthocyanins, polyphenols, triterpenes, steroids, saponins, tannins and phlobatannins, anthraquinones and phlobatannins[30,31]. *Pleopeltispolylepis* is a fern used in the traditional Mexican medicine to treat typhoid fever. Aerial parts extracts of *P.polylepis*showed antibacterial activity against both Gram-positive and negative bacteria[33]Then, the resident in Pakistan used several medicinal plants to cure typhoid fever, they are *Capparis decidua Edgew, FicuscaricaForssk, Syzygiumcumini L., Ziziphusjujuba Mill.*Previous study notified that *Capparis decidua, Ficuscarica, Syzygiumcumini*, and *Ziziphusjujuba* had potent antibacterial agent against *E. coli, S. typhi*, and *P. aeruginosa* which comprising respectable quantity of tannins, flavonoids, steroids, alkaloids, and saponins[34]. Root extract of*Baptisiatinctoria*has been established to bepotent medicine for typhoid treatment[35]. From India, medicinal plants reported effective for typhoid fever were*Fagoniacretica*and *Ocimum basilicum*[36,37].

A total of 26 different worldwide medicinal plants belonging to the 23 families were reported for typhoid fever. Most of them are originated from African continent, India and Pakistan. The parts of medicinal plants used as antisalmonellaare leaves, barks, roots,flowers, fruits, seeds and aerial parts.Antisalmonella activity is mostly identified by in vitro (MIC and MBC). Generally, the chemical compounds contained in the plants are alkaloid, flavonoid, saponin, tannin, phenols, glycosides, steroid and terpenoid; and also in narrow count are oleanolic acid, oleic acid, eicosyl ester, linoleic acid and eugenol.

Several Natural Chemical Compounds of Medicinal Plants and Their Probable Mechanism of Antimicrobial Action.

The mechanism of action by which some medicinal plants exert their antibacterial is not well studied[18]. Many mechanisms of antimicrobial action of phytochemicals have been argued by different researchers, contended that phytochemicals may act by impeding microbial growth, leading cellular membrane disturbances, disruption certain microbial metabolic processes, modulation of signal transduction or gene expression pathways[38]. This study reviews probable mechanism of action of chemical compound contained in medicinal plants. Saponins might confer by revamping the permeability of cell walls and consequently exert toxicity on all organized tissues and by integrating with cell membranes to obtain cell morphology changes leading to cell lysis[30,37]. Polyphenols such as gallic acids act possibly by binding to bacterial dihydrofolatereductase enzymes, inducing topoisomerase IVenzyme-mediated DNA cleavage and bacterial growthstasis, mediation of solute transport inhibition in membranes and affect the phospholipid membranes of bacterial cell wall[18,38]. The antimicrobial properties of alkaloids probably occur by Inhibiting nucleic acid synthesis, the type II topoisomerase enzymes and respiratory system[39,40].The antimicrobial effect of tannins have been demonstrated to bind cell walls of ruminal bacteria, thereby inducing bacterial stasis and protease activity, Inducing topoisomerase IVenzyme-mediated DNA cleavage and inhibition of oxidative phosphorylation[30,31,37]. Flavonoids are synthesized by plants in response to microbial infection. Their antimicrobial activity is probably due to their potential to form complexes with extracellular and soluble proteins as well as the complexation with bacterial cell walls, thereby inducing microbial cell membrane disruptions[30,37].

CONCLUSION

The results of the present review showed that 26 worldwide medicinal plants belonging to 23 families have been reported as antimicrobial for typhoid fever. There were five chemical compound explained their mechanism of action. These results redound to the alternative and complementary medication of typhoid fever and drug discovering of antisalmonella from worldwide medicinal plants. Further research is greatly necessary for characterization of chemical compound or secondary metabolite product of these medicinal plants and investigation their mechanism of action.

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REFERENCES

1. Murray CJ, Vos T, et.al. Disability adjusted life years (DALYs) for 291 diseases and injuries in 21 regions, 1990-2010: a systematic analysis for the Global Burden of Disease Study 2010. Lancet 380:2197–2223.
2. Crump J.A, Sjölund K. M, et al. Epidemiology, Clinical Presentation, Laboratory Diagnosis, Antimicrobial Resistance, and Antimicrobial Management of Invasive Salmonella Infections. ClinMicrobiol Rev doi:10.1128/CMR. 2015 : 00002-15, pp. 902-36.
3. Rowe B, Ward LR, Threlfall EJ. Treatment of multiresistant typhoid fever. Lancet 1991; 337:1422.
4. Barnass S, O'Mahony M, et al. The tangible cost implications of a hospital outbreak of multiply-resistant salmonella. Epidem. Inf. (1989), 103, 227-234 Printed in Great Britain.
5. Mahesh B, Satish S. Antimicrobial activity of some important medicinal plants against lant and human pathogens. World J Agric Sci. 2008.;4:839–43.
6. Davidson-Hunt I. Ecological ethno botany: stumbling toward new practices and paradigms. MASA J. , 2000 : 16:1–13.
7. UNESCO. Culture and Health, Orientation Texts – World Decade for Cultural Development 1988 – 1997. Document CLT/DEC/PRO – 1996, Paris, France, pgs. 129.
8. UNESCO. Terminal Report: Promotion of Ethno botany and the Sustainable Use of Plant Resources in Africa. Document FIT/504-RAF-48, Paris, France, 1998: pgs. 60.
9. Singh R. 2015. Medicinal plants: A review. Journal of Plant Sciences 2015; 3(1-1): 50-55.
10. Lucy Hoareau and Edgar J. DaSilva,:Medicinal plants: a reemerging health aid. Division of Life Sciences UNESCO.
11. Gatsing D, Mbah JA, et al. An antisalmonellal agent from the leaves of GlossocalyxbrevipesBenth (Monimiaceae). Pakistan Journal of Biological Sciences 2006; 9(1): 84-87.
12. Gatsing D, Nkeng PEA et al. Antisalmonellal properties and acute toxicity study of Erythrinaklainei Pierre (Fabaceae) bark extracts and fractions. Res Rev Biosci 2007b. : 1(1):35–41
13. Cheesbrough M. Medical Laboratory Manual for Tropical Countries: Microbiology. ELBS Edition; 1991: pp. 196-205.
14. WHO. Research Guidelines for Evaluating the safety and efficacy of herbal medicines. Manila. Meeting of the working group on the safety and efficacy of herbal medicine/ World Health Organization, Geneva. 1992.
15. Karo M, Tambaip T, Hatta M, et al. A Mini Review of Indonesian Medicinal Plants for Vulvovaginal Candidiasis.Rasayan J. Chem. 2017. :Vol. 10, No. 4, 1280-1288.
16. TuanDo Q, Bernad P. Reverse pharmacognosy: a new concept for accelerating natural drug discovery. Elsevier : 2006.
17. Awodele, O, Daniel A, et al. Study on pharmacovigilance of herbal medicines in Lagos West Senatorial District, Nigeria. International Journal of Risk & Safety in Medicine, 2013. :vol. 25, no. 4, pp. 205-217.
18. Megeressa M, Bisrat D, et al. Structural elucidation of some antimicrobial constituents from the leaf latex of Aloe trigonantha L.C. Leach.Megeressa et al. BMC Complementary and Alternative Medicine (2015) 15:270 DOI 10.1186/s12906-015-0803-4.
19. Lunga P.K, Gatsing D, et al. Antityphoid and radical scavenging properties of the methanol extracts and compounds from the aerial part of Paulliniapinnata. SpringerPlus, 2014. :3:302.
20. EbiHYPERLINK "https://www.ncbi.nlm.nih.gov/pubmed/?term=Ebi%20GC%5BAuthor%5D&cauthor=true&cauthor_uid=11180528" GC, KamaluHYPERLINK "https://www.ncbi.nlm.nih.gov/pubmed/?term=Kamalu%20TN%5BAuthor%5D&cauthor=true&cauthor_uid=11180528"TN.Phytochemicalandantimicrobial properties of constituents of "OgwuOdenigbo", a popular Nigerian herbal medicine for typhoid fever. Phytother Res. 2001 Feb;15(1):73-5.
21. Nkuo-AkenjiHYPERLINK "https://www.ncbi.nlm.nih.gov/pubmed/?term=Nkuo-Akenji%20T%5BAuthor%5D&cauthor=true&cauthor_uid=12201022" T, NdipHYPERLINK "https://www.ncbi.nlm.nih.gov/pubmed/?term=Ndip%20

R%5BAuthor%5D&cauthor=true&cauthor_uid=12201022" R, et al. Anti-Salmonella activity of medicinal plants from Cameroon. Cent Afr J Med. 2001 Jun;47(6):155-8.

22. Krisna KL, Paridravi M, et al. Review on Nutritional, Medicinal and Pharmacological Properties of Papaya (Carica papaya Linn.). Natural Product Radiance, 2008: Vol.7 (4), pp. 364-73.
23. N'guessan J D, Coulibaly A, et al. Antibacterial activity of Thonningiasanguinea against some multidrug resistant strains of Salmonella enterica. African Health Sciences 2007; 7(3):155-158.
24. Waage SK, Hedin PA. Biologically-active flavonoids from Gossypium arboretum.Elsevier :Phytochemistry, Volume 23, Issue 11, 1984, Pages 2509-2511.
25. Evans CE, Banso A, Samuel OA. Efficacy of some nupe medicinal plants against Salmonella typhi: an in vitro study. J of Ethnopharmacology, Volume 80, Issue 1, April 2002, Pages 21-24.
26. Ciraj AM, Sulaim J, et al. Antibacterial activity of black tea (Cameliasinensis) extract against Salmonella serotypes causing enteric fever. Indian J Med Sci. 2001. : 55(7):376-81.
27. Ateufack G, Nguelefack TB, et al. Antiulcer effects of the aqueous and organic extracts of the stem bark of Anthocleistavogelii in rats. Pharmaceutical Biology 2006. 44(3): 166–171.
28. AnyanwuHYPERLINK "https://www.ncbi.nlm.nih.gov/pubmed/?term=Anyanwu%20GO%5BAuthor%5D&cauthor=true&cauthor_uid=26432351" GO, Nisar-ur-Rehman, et al. Medicinal plants of the genus Anthocleista--A review of their ethnobotany, phytochemistry and pharmacology. J Ethnopharmacol. Elsevier Ireland Ltd . 2015 Dec 4;175:648-67.
29. Jensen, SR, Schripsema, J, Chemotaxonomy and pharmacology of Gentianaceae. In: Struwe, L. & Albert, V. (Editors). Gentianaceae - Systematics and Natural History. Cambridge University Press, United Kingdom. 2002.: pp. 573–631.
30. Gatsing D, Adoga GI. Antisalmonellal Activity and Phytochemical Screening of the Various Parts of Cassia petersianaBolle (Caesalpiniaceae).Research Journal of Microbiology 2007.: 2(11):876-880.
31. Bosch, CH. SennapetersianaBolle Lock. Record from Protabase. Prota, Netherlands. 2007.
32. AkinyemiHYPERLINK "https://www.ncbi.nlm.nih.gov/pubmed/?term=Akinyemi%20KO%5BAuthor%5D&cauthor=true&cauthor_uid=16093235" KO, MendieHYPERLINK "https://www.ncbi.nlm.nih.gov/pubmed/?term=Mendie%20UE%5BAuthor%5D&cauthor=true&cauthor_uid=16093235" UE, et al. Screening of some medicinal plants used in south-west Nigerian traditional medicine for anti-Salmonella typhi activity. J Herb Pharmacother. 2005;5(1):45-60.
33. Contreras Cárdenas AV, et al. Antimicrobial, cytotoxic, and anti-inflammatory activities of Pleopeltispolylepis. 2016.
34. Shad A, Ahmad S, et al. Phytochemical and Biological Activities of Four Wild Medicinal Plants. Hindawi Publishing Corporation Scientific World Journal, Article ID 857363, 7 pages. 2014.
35. Puri D, Bhandari A. Fagonia: A Potential Medicinal Desert Plant. Journal of NPA, 2014 XXVII (1), pp. 28-33.
36. Hannan A, AsgharHYPERLINK "https://www.ncbi.nlm.nih.gov/pubmed/?term=Asghar%20S%5BAuthor%5D&cauthor=true&cauthor_uid=23811447" S, et al. Antibacterial effect of mango (Mangiferaindica Linn.) leaf extract against antibiotic sensitive and multi-drug resistant Salmonella typhi. Pak J Pharm Sci. 2013 Jul;26(4):715-9.
37. Adeola SA, Folorunso OS. Antimicrobial Activity of Ocimumbasilicumand itsInhibition on the Characterized and Partially Purified Extracellular Protease of Salmonella typhimurium. Research J of Biology (2012), Vol. 02, Issue 05, pp. 138-144.
38. OmojateGC ,Enwa FO. Mechanisms of Antimicrobial Actions of Phytochemicals against Enteric Pathogens – A Review. J of Pharmaceutical, Chemical and Biological Sciences ISSN: 2348-7658; 2014.: 2(2):77-85.
39. Tominaga K, Higuchi K, et al. In vivo action of novel alkyl methyl quinolone alkaloids against Helicobacter pylori. J AntimicrobChemother 2002; 50:547-552.
40. Cushnie TP, CushnieB. Alkaloids: An overview of their antibacterial, antibiotic-enhancing and antivirulence activities.Int J of Antimicrobial Agents 2014:44(5). DOI: 10.1016/j.ijantimicag.2014.06.001.