Medicinal plants as an alternative therapeutic source against *Salmonella*

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**ABSTRACT**

Medicinal plants are found to be effective in the treatment of various diseases. These activities could be due to the presence of primary and secondary metabolites. A lot of efforts was taken related to this medicinal plant and studied various disease model-based studies. One of the diseases, i.e., *Salmonella* (gram-negative; non-sporing bacterium; family *Enterobacteriaceae*), a bacterial disease mainly affects on the gastrointestinal tract. This bacterium survives in human intestines and is shed through feces. Generally, this infection is reported in humans through the intake of contaminated water/food and also caused through eating raw or undercooked meat, poultry and egg products. These products may be responsible for causing diarrhea, abdominal pain and fever. In India, approximately 500 children suffer from typhoid per 100,000, in the age group of 5-15 years. This disease showed a significant burden among young children and also showed several complications also reported due to *Salmonella* diseases, i.e., dehydration, bacteremia, reactive arthritis, etc. In contrast, *Salmonella* grows at a particular pH range between 4 to 8 and the maximum temperature that are required for the growth between 8 to 45 degree Celsius. In literature, about 2500 serotypes and five different strains (*Salmonella Enteritidis, Salmonella Typhimurium, Salmonella Newport, Salmonella Javiana and Salmonella Heidelberg*) have been reported. The objective of our study is to collect the information related to *salmonella* and also understand its correlation between *Salmonella* and medicinal plant products.

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**INTRODUCTION**

An ethnobotanical survey related to medicinal plants was carried out in India and other neighboring countries where it will be mentioned the usage of these medicinal plants provide some beneficial effect against various infectious diseases (*Lulekal et al., 2008; Chekole, 2017*). Collect the information as well as literature was obtained from villagers, including traditional healers, having some knowledge related to medicinal plants (*Gupta et al., 2016, 2017*). In literature, medicinal plants are primarily used for human health care related to the treatment of many opportunistic infections. Various studies were conducted by researchers and reported various immunopharmacological activities (*Gupta and Shah, 2016; Gupta and Chaphalkar, 2016a*). These activities could be due to the presence of active ingredients, particularly seen in case of plant extracts/fractions or pure molecules with antimicrobial properties and also considered as one of the anti-pathogenic bacterial compounds after separation and complementary pharmaceutical stud-
ies (Shaikh et al., 2016; Gupta and Chaphalkar, 2016b). In view of this, we collected the literature about *Salmonella* and studied its various species, including mechanism of action (Galán, 2016), which may directly or indirectly affects on human health-care. In this regard, a wide range of immunopharmacological studies were conducted related to antibacterial effects (*Salmonella* species) of medicinal plant extracts, including their active ingredients and used in traditional medicine pertaining to control the burden of bacterial growth including food spoilage. The major objective of our study is about scientific research approach related to plants containing bioactive substances and sources of potentially useful chemicals but only a fraction of them have been used in medicine against *Salmonella* disease.

One of the bacterial diseases, i.e., *Salmonella* firstly identified as a human pathogen in the 19th century, which is mainly reported in the intestines of birds and humans. Generally, this bacteria is mainly contaminated food materials and targeted people, especially children, because of weakened immune systems with a higher risk of illness (Galán, 2016; Roberts et al., 2009). The symptoms (fever, abdominal cramps, etc.) should appear within 12 to 72 h after consuming contaminated food materials. In most of the cases, people will recover without any complications, but only in rare cases, patients will severely dehydrated and the infection goes directly into the bloodstream. In literature, approximately 2000 strains of *Salmonella* species were reported and categorized them on the basis of a specific antigenic set called as serotypes. The most common and available strains of Salmonella (Galán, 2016; Roberts et al., 2009; Soto, 2006) are *Salmonella* Enteritidis, *Salmonella* typhimurium, *Salmonella* Newport, *Salmonella* Javiana and *Salmonella* Heidelberg. In this regard, two widely commercially available vaccines licensed for human use against *Salmonella*, i.e., live attenuated vaccine, Ty21a and Vi capsular polysaccharide (Vi CPS). In contrast, the *Salmonella* genome contains several clusters of genes, referred to as *Salmonella* pathogenicity islands (SPIs) that encode a number of virulence factors, i.e., SPI-1 (genes required for bacterial entry); SPI-2 (necessary for intracellular survival). Although the functional boundaries between the two have recently become less distinct. Both SPI-1 and SPI-2 encode type III secretion systems (T3SS), a sort of molecular syringe consisting of more than 20 proteins that spans both inner and outer bacterial membranes and inserts into the plasma membrane of the host. This sophisticated apparatus, which is evolutionarily conserved among many Gram-negative pathogens, mediates the translocation of bacterial virulence factors into the host cell cytosol (Soto, 2006; Collinson et al., 1996; Ahmed et al., 2000).

This *Salmonella* disease is considered a major health problem in the world, especially in developing countries, including India. Generally, *Salmonella* is mainly associated with poultry products (fruits, vegetables, dog food, etc.) and this disease will occur in humans in the form of food infection, gastroenteritis, typhoid fever and sometimes septicemia. As *Salmonella* strains are so much similar, number of methods are applied and currently used as well as applied in order to distinguish between outbreak strains especially physiological characteristics of the organisms, i.e., flagella and cell wall (Soto, 2006; Collinson et al., 1996; Ahmed et al., 2000). However, immunological and molecular level based studies should be required to determine the expression and immunogenicity of bacterial genes. In addition, studies were conducted related to high-throughput DNA-based approach with respect to *Salmonella* serotyping. With reference to this approach, *Salmonella* strains (224) were characterized, including reference strains, medically relevant strains and 18 strains deemed non-typeable by traditional methods. In view of this, the technique showed more potential pertaining to replace more labor-intensive traditional approaches, making it quicker to identify disease-causing strains of *Salmonella* and the source of future outbreaks (Collinson et al., 1996; Ahmed et al., 2000). A lot of efforts were also made in order to control the burden of *Salmonella* disease using medicinal plant products. Therefore, there is a need to develop alternative antimicrobial drugs extracted from medicinal plant products for the treatment of infectious diseases.

**RESULTS AND DISCUSSION**

Following are the examples related to medicinal plants against *Salmonella* as shown below,

One of the traditionally used medicine, *Glycyrrhiza* glabra (Licorice and sweet wood; family *Papilionaceae*) and *Azadirachta indica* (Neem, family *Meliaceae*) having antibacterial activity was reported. In *Glycyrrhiza* glabra, contained one of the phytochemicals, i.e., saponin glycoside(*glycyrrhizin*), whereas neem seeds contained azadirachtin and also reported other secondary metabolites (flavonoids, terpenoids, saponin, etc.). Both these medicinal plants, i.e., licorice stem and neem seeds using methanol as a solvent system and these may showing a broad spectrum of antityphoidal activity. In other words, herbal extracts of...
these medicinal plants used in humans may prevent or control the burden of typhoid disease. Overall, these medicinal plants are used in the form of traditional medicine pertaining to cure a common ailment, i.e., typhoid (Nassiri-Asl et al., 2007; Gulet et al., 2015).

In Andrographis paniculata and Aloe vera, the medicinal plant reported worldwide and showed various immunopharmacological properties, especially antibacterial activity were observed in plant leaves (petroleum ether, diethyl ether, chloroform and methanol) against gram-positive and gram-negative bacteria using disc method. The maximum antimicrobial activity was reported on the basis of the diameter zone of inhibition in Andrographis paniculata and Aloe vera (methanol extract) using various concentrations. In this study, Salmonella Typhimurium was cultured using medium (MacConkey) and confirmed their presence through culturing on TSI agar and urea agar base and tested for H2S production and pink color formation in TSI and a negative result for urease activity in urea agar medium. From these studies, authors claimed that methanolic extract of these medicinal plants, especially leaves showed anti-Salmonella based activity. Overall, its major concern is about the development of natural antimicrobials obtained from medicinal plant products pertaining to the control foodborne and spoilage microorganisms (Hussain and Kumaresan, 2013).

In Piper betle, medicinal plant products, especially leaves in the form of aqueous extract has shown its ability (in vitro and in vivo) inhibit the growth of Salmonella. In this extract, the presence of alkaloids, flavonoids, steroids, triterpenoids and phenolic hydroquinones were present. This activity is due to the presence of an anti-salmonella component (i.e., sterols, e.g., karvakrol and eugenol) is reported in beetle extracts. In addition, beetle leaves extract showed antimicrobial, anti-oxidative and anti-hemolytic effects and also used as a natural antibiotic applied in poultry farms in some countries. In some cases, aqueous extraction methods does not show any type of inhibition zone in some of the Salmonella colonies. In this regard, the proper method is applied for aqueous extraction methods that could bring better results as compared to ethanolic extracts. Some of the aqueous extraction methods of plants showed a better result than ethanolic extraction methods (Widjay et al., 2017).

Medicinal plants are mainly used for the development of antibiotics and played an important role in the treatment of Salmonella disease, i.e., typhoid fever (bacterial infection; Salmonella typhi/Salmonella paratyphi) (Contreras et al., 1997). One of the studies related to medicinal plants, i.e., Alchornealaxiflora, Ageratum conyzoides and Spondiamombin were observed and confirmed the presence of secondary metabolites (i.e., tannin, steroid, phenol, saponin, phibatanin and flavonoid). In addition, minerals (Na, K, Ca, Mg, Zn and Fe) are also reported. All these plants showed antibacterial activity against Salmonella typhi/ Salmonella paratyphi using the agar diffusion method. From these studies, the author suggests that these medicinal plants (Alchornealaxiflora, Ageratum conyzoides, and Spondiamombin) were effective against typhoid fever infection (Osuntokun and Olajubu, 2015).

Medicinal plant products (roots, leaves, and in orescence of E.hirta; roots of C.occidentalisand leaves, stem and inflorescence of C. eucalyptus) were used and claimed its antibacterial effect (Salmonella typhi) using agar ditch method. Firstly, phytochemical investigations of E. hirta reveals the presence of saponin in roots and tannin in roots, stems and inflorescence but glycosides and alkaloids are totally absent; C. occidentalis reveals the presence of saponin and tannin whereas C. eucalyptus reveals the presence of alkaloid, saponin and tannin. In short, these medicinal plants are so much effective against Salmonella typhi, and only C. eucalyptus contains the natural compound that can be used in the treatment of typhoid fever (Evans et al., 2002).

Antimicrobial activity of different plant extracts (Piper betle, Boerhaviadiffusa, Oxalis corniculata, Camellia sinensis, Curcuma longa and Allium cepa) were prepared using the different solvent system and claimed its effect against Gram-negative bacterial species (Salmonella sp.) on the basis of a zone of inhibition through disc diffusion method. In comparison with these six plants, only Camellia sinensis and Piper betle was found to be more effective against Gram-negative bacteria (e.g., Salmonella species). This study deserves more extensively work on isolation and identification of active ingredients from these tested medicinal plants having antibacterial properties in order to explore its potential in the treatment of many infectious diseases. Overall, these medicinal plants should be considered as a good source for herbal drugs (Lijon, 2016).

Medicinal plant extracts (i.e., Tithoniadiversifolia, Warburgiaagandensis, Croton megalocarpus, Carissa edulis, andLaunaecornuta) traditionally used for anti-Salmonellaand confirmed its activity through disc diffusion and microdilution techniques. In other words, these medicinal plant-based extracts with anti-Salmonella activity should be used as a
source of antibiotic substances that may be applied useful in the treatment of Salmonella diseases. This study should provides the scientific basis for the traditional application against typhoid fever (Peter et al., 2015).

CONCLUSIONS

Medicinal plants should be considered as one of the most potential sources of chemicals, but only a few of the fractions may have been used for medicinal purposes. In an effort to eliminate this infectious disease, i.e., Salmonellae, various types of alternative therapeutic methods are applied, i.e., usage of medicinal plant products. Several biological scientists from different fields around the world have researched on this particular infectious disease and came up with an interesting type of results conclusion as mentioned above, which demonstrated the activity of various medicinal plant products in the treatment of salmonellosis diseases, especially reported in poultry and cattle gastrointestinal diseases. In short, a potency of medicinal plant-based extracts against Salmonella was not due to the presence of primary or secondary metabolites but possibly through another mechanism of action. Further studies were conducted related to its mode of action of these plant-based extracts against Salmonella species and resistant clinical strains. Hopefully, isolation and identification of active ingredients can be produced and entered in the pharmaceutical market as anti-Salmonella drugs.

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