

**SCREENING AND IDENTIFICATION OF
POTENT ANTIMICROBIAL CONSTITUENTS
FROM SELECTED MYANMAR MEDICINAL
PLANTS USED IN THE TREATMENT
OF TYPHOID**

PhD (DISSERTATION)

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ABSTRACT

The main aim of this work was to screen and develop a herbal drug that can be used in the treatment of typhoid fever caused by *Salmonella* species. Anti-*Salmonella* activity of different plants including *Aristolochia indica* Linn. (Eik-thara-muli) roots, *Plumbago rosea* Linn. (Kant-gyoke-ni) roots, *Cissus discolor* (Ta-bin-taing-mya-nan) rhizome and *Semicarpus anacardium* (Chay-thee) fruit extracted by various solvents, were tested against *S. typhi*, *S. paratyphi*, *S. krefeld*, *S. choleraesuis*, *S. enteritidis*, *S. derby* and *S. stanley* by agar disc diffusion and microbroth dilution assays. The results obtained show strong activity of the petroleum ether (PE) and ethyl alcohol (EtOH) extracts of *P. rosea* and mild activity of EtOH extract of *A. indica* against bacteria used as test organisms. Minimal Inhibitory Concentration (MIC) values of each active extracts were determined and found that PE extract of *P. rosea* ranged from 125-500 μ g/mL and ethyl acetate soluble portion of EtOH extract of *P. rosea* ranged from 250-1000 μ g/mL.

Isolation, solvent partition, successively column chromatographic separation and crystallization provided plumbagin (1) (0.31% yield, m.p.=76-78°C), β -sitosterol (2) (0.02% yield, m.p.=140-142°C) and isoshinanolone (3) (0.03% yield) from active PE extract of *P. rosea* and aristolochic acid (4) (0.16% yield, m.p.=268°C) from active EtOH extract of *A. indica*. All isolated compounds were identified or characterized by their melting points, UV, FT-IR, ^1H - and ^{13}C -NMR and EIMS spectra.

Plumbagin (1) showed the most potent anti-*Salmonella* activity (inhibition zone=15-29mm against different *Salmonella*) which is comparable to tetracycline drug control (inhibition zone=18-28mm against different *Salmonella*). Furthermore, the activity of 1 is higher than that of PE crude extract of "Kant-gyoke-ni". Aristolochic acid (4) also showed anti-*Salmonella* activity (inhibition zone=20mm against *S. typhi*), however, the activity was lower than 1. In addition, the activity is similar to that of EtOH crude extract.

Microbroth dilution assays revealed the MICs of **1** at 100µg/mL against *S. typhi*, *S. derby*, *S. paratyphi*, *S. krefeld*; >100µg/mL against *S. stanley*, *S. choleraesuis* and *S. enteritidis*; 50µg/mL against *E. coli* and 25µg/mL against *Staphylococcus aureus*.

Present investigation revealed that either crude plants or PE extract of “Kant-gyoke-ni” or EtOH extract of “Eik-thara-muli” could be used as a remedy for typhoid fever as claimed by Myanmar traditional medicinal practitioners. Indeed, PE extract of “Kant-gyoke-ni” may be more effective than EtOH extract of “Eik-thara-muli”. However, “Ta-bin-taing-mya-nan” and “Chay-thee” have not shown such activity in *in vitro* anti-*Salmonella* activity assays.

The anti-*Salmonella* activity of **1** is higher than that of PE crude extract of “Kant-gyoke-ni”. Thus, **1** could be the main constituent of the plant responsible for its activity and may be of therapeutic value in treating typhoid fever. In addition, **1** could be considered as a promising antimicrobial agent. The first finding in Myanmar for plumbagin **1** as anti-*Salmonella* a potent remedy from plant origin will be a great advancement in bacterial infection therapies.