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A Review on the Evaluation of Antimicrobial Properties of Crude Extracts and Bioactive Compounds Derived from *Andrographis paniculata*

Fikri Haziq Zaidi and Siti Hasmah Mohtar*

Department of Science and Biotechnology, Faculty of Engineering and Life Sciences, Universiti Selangor, Jalan Timur Tambahan, 45600 Bestari Jaya, Selangor
hasmah@unisel.edu.my

Abstract

Medicinal plants have been used as traditional medicines to cure several infectious diseases. Various plant extracts and bioactive compounds of medicinal plants have shown potential as antimicrobial agents against bacteria, fungi and viruses. *Andrographis paniculata* is one of the valuable medicinal plants that possess a variety of pharmacological properties. The present study aimed to evaluate the potential of *Andrographis paniculata* as an antimicrobial agent based on data gathered from previous scientific studies. This study had focused on the efficacy of the *Andrographis paniculata* crude extracts and their bioactive compounds as an antimicrobial agent against selected pathogenic microbes. The efficacy of *Andrographis paniculata* as an antimicrobial agent was influenced by the type of solvent used for the extraction of crude extracts. The methanol extract of *Andrographis paniculata* leaves exhibited the most significant antibacterial activity against several bacterial species. Furthermore, several bioactive compounds isolated from *Andrographis paniculata* demonstrated a significant role in inhibiting microbial activity. A bioactive compound identified as andrographolide has been recognized as a potential antimicrobial agent that possesses a variety of inhibitory effects against selected pathogens. The current findings indicate that *Andrographis paniculata* has potent antimicrobial properties either as a plant crude extract or isolated as a bioactive compound.

Keyword: *Andrographis paniculata*; antimicrobial agent; crude extracts; bioactive compounds

INTRODUCTION

Andrographis paniculata or in Malay known as 'hempedu bumi' is one of the medicinal plants that have been used traditionally to treat several diseases. The whole plant including the shoots, leaves and roots are used traditionally as powder, infusion, or decoction form either alone or in combination with other medicinal plants for the treatment of diseases such as leprosy, gonorrhoea, respiratory tract infections, scabies, boils, skin eruptions, chronic and seasonal fevers, irregular bowel habits, diabetes, jaundice, dyspepsia, cough, oedema, liver complaints,

dysentery, malaria, enteritis, helminthiasis, herpes, peptic ulcer and skin infections [1]. Different extracts such as acetone, chloroform, ethanol, hexane, methanol or even aqueous as well as isolated bioactive compounds from plant parts of *Andrographis paniculata* have been studied for pharmaceutical properties such as antibacterial, antiviral, antifungal, antiparasitic, choleretic, hypocholesterolemia, anti-inflammatory, anti-hyperglycemic, hepatoprotective, anticancer, immunomodulator, cardiovascular, antihyperlipidemic, emollients, anti-snake venom, anti-platelet aggregation, anti-fertility, carminative, and antipyretic properties in vitro and in vivo [2].

The plant contains diterpenoids, flavonoids and polyphenols as the major bioactive components [3,4]. Andrographolide ($C_{20}H_{30}O_5$) is the major diterpenoid in *A. paniculata*, making up about 4%, 0.8~1.2% and 0.5~6% in dried whole plant, stem and leaf extracts respectively [5,6]. The other main diterpenoids are deoxyandrographolide, neoandrographolide, 14-deoxy-11,12-didehydroandrographide and isoandrographolide [5,6]. *A. paniculata* extracts and their bioactive molecules were investigated against a wide variety of pathogens, including several antibiotic-resistant species including *Staphylococcus aureus*, *Pseudomonas aeruginosa*, *Shigella* spp., *Salmonella* spp., *Candida* spp., and *Streptococcus pneumoniae*. A total of 59 invasive microbes have been used to investigate the antimicrobial efficacy of *A. paniculata* extracts together with their isolated pure compounds as reported previously [7]. Therefore, the present study was aimed to determine the efficacy of the crude extracts of *Andrographis paniculata* and its bioactive compounds as antimicrobial agent to treat diseases associated with bacterial and viral infections.

METHODOLOGY

The present study involves gathering of information from previous studies mainly from the journal papers within the scope of study. Primary data was obtained from worldwide accepted scientific databases including PubMed, Science Direct, Researchgate, and NCBI. The relevant data were compiled and analyzed in order to determine the most effective crude extracts and bioactive compounds that demonstrate the antimicrobial properties against variety of microorganisms. Readings and evaluations have been used as a strategy for summarizing data. All of the data have been compiled and summarized in order to complete this review.

RESULT AND DISCUSSION

Evaluation of *Andrographis paniculata* crude extracts as antimicrobial agent

The aqueous extract of *A. paniculata* showed significant antibacterial activity, which was further linked to the presence of andrographolides and arabinogalactan proteins [8]. A significant activity against the Gram-positive *S. aureus*, MRSA, and Gram-negative *P. aeruginosa* was reported by crude water extracts of leaves sample [10]. However, the crude water extract of *A. paniculata* leaves exhibited no effect on *E. coli* and *K. pneumoniae*. Furthermore, no antimicrobial effect of the aqueous extracts of the whole plant and isolated andrographolide on tested common pathogenic bacteria. Methanol extract of leaves showed significant activity against *E. coli* along with *P. aeruginosa*, *K. pneumonia*, *S. aureus*, *B. subtilis* and *Streptococcus epidemidis* [11]. Previous studies have shown that methanol extract of *A. paniculata* leaves exhibited strong in vitro antibacterial activity against bacteria including clinical isolates of *Staphylococcus aureus, Edwardsiella tarda, E. coli, Flavobacterium sp. P. aeruginosa, E. faecalis, S. saprophyticus, B. subtilis* and *Proteus vulgaris*. Phytochemical investigations of thin layer chromatography (TLC) purified active fraction from this extract showed the presence of terpenoids [13]. Similarly, the potent inhibitory effect of ethanol extract

of aerial parts on the growth of both Gram-positive and Gram-negative bacteria, namely, *Salmonella typhi*, *V. cholera*, *V. alginolyteus*, *S. aureus*, *Shigella boydii*, *Shigella sonnei*, *E. coli*, *B. licheniformis*, and *Salmonella typhimurium* [15]. However, ethanol extracts were found effective against *Legionella pneumophila* and *Bordetella pertussis* only. These findings indicated that the extraction process and solvent have a significant role in the efficacy of *A. paniculata* as the number and yield of pure metabolites greatly differ depending on the types of fractions.

Evaluation of *Andrographis paniculata* bioactive compounds as antimicrobial agent

Andrographolide, neoandrographolide and isoandrographolide are the most abundant lead bioactive compounds that can be isolated from any part of *A. paniculata* [10]. A total of 35 isolated compounds have been tested for antimicrobial activities, of which 20 secondary metabolites showed antimicrobial effects [7]. Antimicrobial metabolites were extracted from the whole plant, aerial part, leaves and roots. Previous study [13] reported that the co-presence of andrographolide and arabinogalactan proteins in the ethanol extract was further acknowledged for its enhanced antibacterial activity compared to andrographolide and arabinogalactan proteins alone. A total of 13 pure secondary metabolites of *A. paniculata* have been reported [7] to have significant antibacterial effects (e.g. Andrographolide, Isoandrographolide, 14-deoxyandrographolide, 14-deoxy-11 and 12-didehydroxiandrographolide). These compounds have been used to evaluate antibacterial potency against a wide range of bacteria. Overall, Gram-positive bacteria were more susceptible to andrographolide than Gram-negative bacteria due to the presence of the outer membrane and the polarity nature of the compound. Among the selected metabolites, andrographolide, 14-deoxy-11, 12-didehydroxiandrographolide and andrograpanin exhibited significant antibiofilm effects against *P. aeruginosa* [16] and *S. aureus* [17]. The role of andrographolide and neoandrographolide in treating bacillary dysentery caused by *Shigella sp*. was reported in several studies [9]. Andrographolide has an antibacterial effect on a wide variety of bacteria, which is reflected in the inhibition of bacterial pathogenic factors and the regulation of immunity to downregulate infectious inflammation caused by bacteria [18].

The andrographolide, it's derivative-14-deoxy-11,12-didehydroandrographolide and semi-synthetic analogue-3,19-isopropylidene andrographolide (IPAD) have been reported demonstrated antiviral effect against HPV16PsV infection [19]. A study had reported considerable inhibitory activity (both in vitro and in vivo) of 14-α′-lipoyl andrographolide (AL-1), a synthetic derivative of andrographolide, against influenza A viruses H5N1, H9N2, and H1N1 [20]. The similar result was observed [21] for 14-acetyl analogues of andrographolides (14-acetyl-3,9-isopropylideneandrographolide,14-acetylandrographolide, 3,14,19 triacetylandrographolide) against HSV-1 in vitro. Andrographolide and 14-deoxy-11,12-didehydroandrographolide also demonstrated significant anti-HIV properties [22]. A recent study had reported on the potential of andrographolide as an inhibitor of the main protease of SARS-COV-2 (Mpro) through in silico studies [23]. Andrographolide was docked successfully in the binding site of SARS-CoV-2 Mpro. Computational approaches also predict this molecule to have good solubility, pharmacodynamics property and target accuracy. Andrographolide can inhibit the formation of bacterial biofilms, the production of virulence factors, the adhesion between bacteria, and the destruction of bacterial integrity in direct bacteriostatic action. This antimicrobial property of andrographolide and its analogs also exhibits notable properties in combination with antibiotics [18]. Andrographolide can partially restore antibiotic susceptibility by inhibiting the expression of bacterial efflux pumps and competitively inhibiting antibiotic resistance sites in bacteria.

CONCLUSION

Previous studies have shown that *Andrographis paniculata* possess the antimicrobial properties including antibacterial, antiviral, antifungal and anti-inflammatory. The solvents used in the extraction of the crude extracts had influence the components of bioactive compounds and subsequently contributing towards the efficacy against selected microbes. The methanol extract of *A. paniculata* and its bioactive compound, andrographolide had demonstrated the most significant antimicrobial activity against selected pathogens.

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