



Antibacterial Activity of Aqueous Fungal Extracts Derived From Basidiomycetes



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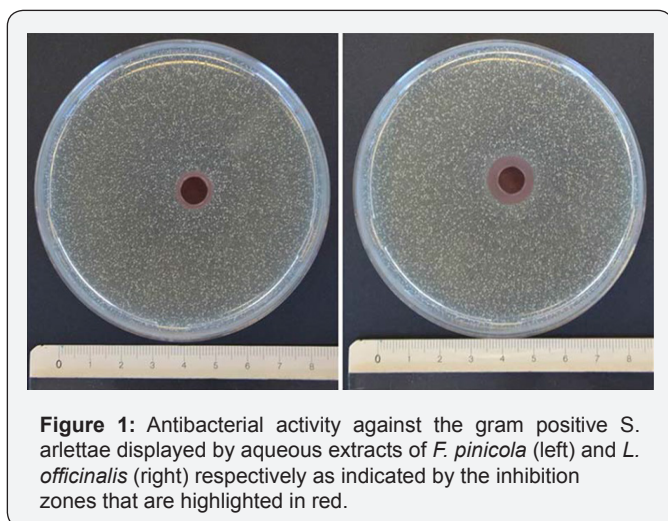
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Commentary

After the discovery of penicillin, β -lactam antibiotics with their broad spectrum of action in combination with low toxicity were commonly used as agents for the treatment of bacterial infections. However their frequent abuse and misuse gave rise to increasing numbers of multi resistant bacteria as a result of adaptation [1]. With infectious diseases being one of the most frequent cause of death worldwide the increase in multi-resistant bacteria clearly poses threat to global health (WHO, 2014). Researchers, as well as pharmaceutical companies have therefore devoted a lot of effort in the search for new antibacterial substances in the fight against the growing resistance [2,3]. A strategy for the discovery of new promising therapeutic agents is ethno pharmacology, which is "the interdisciplinary scientific exploration of biologically active agents traditionally employed or observed by man" [4]. The potential of ethno pharmacology is highlighted by the fact that for small molecule drugs (excluding peptides, proteins and vaccines) marketed between 1981 and 2010 almost 50% of them originated or derived from natural products with numbers rising for agents targeting specific diseases such as anticancer drugs (65%), antibiotics (75%) or antiviral therapeutics (77%) [5,6]. New lead substances thereby are not only found in plants but also in other organisms such as fungi which are a source of a vast amount of different metabolites [7,8]. Two examples of fungal metabolites that made their way into clinical use are camptothecin [9] as a lead molecule for anti-cancer drugs and podophyllotoxin [9] for the topical treatment of warts. Mushrooms have been used for their antibacterial, anti-inflammatory and homeostatic properties long before the onset of modern medicine [10-12]. 'Ötzi' the Iceman who lived 3000 BC in the Tyrolean alps, used pharmaceutical active fungi as a prehistoric "first aid kit" [13,14]. We therefore screened the crude aqueous fungal extracts of nine basidiomycetes including *Fomes fomentarius*, *Fomitopsis pinicola*, *Ganoderma adspersum*,

Ganoderma lucidum, *Ganoderma tsugae*, *Inonotus obliquus*, *Laricifomes officinalis*, *Laetiporus sulphureus* and *Piptoporus betulinus* for their antimicrobial potential. Of the 9 aqueous fungal extracts *F. Pinicola* and *L. officinalis* showed a moderate antibacterial activity against the gram positive model organism *S. arlettae* (Figure 1) while growth of gram negative *E. coli* was not inhibited by any of the extracts. These results are in good agreement with observations made in other studies [15-20] i.e. gram positive bacteria were more susceptible towards fungal extracts than gram negative bacteria such as *E. coli*. It is however difficult to compare results of bioactivity from different studies as there is no general consensus neither on the antimicrobial assay [21] applied such as well diffusion also known as agar cup method [18], disc diffusion method [20], broth micro-dilution [22], *in vivo* [23], with which the organisms were tested nor on the production of the fungal extracts and fractions under investigation. Furthermore proper species identification is often neglected [24]. As a result findings in the literature are often discussed in terms of relative trends rather than absolute values. Nevertheless, the poor antibiotic performance demonstrated in this study should not be mistaken for an antimicrobial inefficiency of fungal extracts in general especially taken into account three important considerations. First crude aqueous extracts as applied in this case are always mixtures of active and non-active compounds and as such might be outperformed by their chromatographic fractions [6,25,26] Secondly, water is considered to be a non-solvent for most of the pharmaceutically active constituents including sterols, terpenoids, alkaloids, polyphenols, flavones or lactones commonly found in higher quantities in low polarity organic solvents, while on the other hand it serves almost exclusively as solvent for fungal derived polypeptides and polysaccharides [22,24]. Such substances however, although known for their antimicrobial properties [19,23,26-28], might not reveal their antimicrobial potential in

diffusion based assays as a result of their high molecular weight [29,30]. Thirdly the presence and quantity of pharmaceutically active metabolites in fungi might vary strongly depending on external factors. Various reports have shown the production of metabolites to be substrate dependent [31-34]. In fact the occurrence of certain metabolites might only be observed in the presence of a distinct host [35]. In summary two of the crude aqueous fungal extracts did show a moderate activity against *S. arlettae* a model organism for gram positive bacteria while none of the extracts tested exhibited an activity against the gram negative *E. coli*. Nevertheless the antimicrobial potential of basidiomycetes has been demonstrated in countless studies and the reason they did not make their way from naturopathy into clinical practice yet is mostly related to their slow growth rates and low product yields compared to other more proliferative sources such as streptomycetes [15]. Evidence for the pharmaceutical potential inherent to basidiomycetes is the agent pleuromutilin [36,37] a lead substance for a new class of antibiotics nowadays approved for applications in humans and animals.



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