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Tropical ulcer plant treatments used by Papua New Guinea's Apsokok nomads

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ABSTRACT

Ethnopharmacological relevance: The tropical ulcer is a debilitating bacterial infection that is common in Papua New Guinea. Deploying healthcare infrastructure to remote and inaccessible rainforest locations is not practical, therefore local plants may be the best treatment option. Here we present an ethnobotanical survey of the tropical ulcer plant medicines used by the semi-nomadic Apsokok who roam the remote central mountains of Papua New Guinea's West New Britain Province. *In vitro* biological activity in assays relevant to tropical ulcer wound healing is also presented.

Materials and methods: Focus groups and semi-structured interviews were used to acquire information on the uses of plants, vouchers of which were identified by comparison with authentic herbarium specimens. Antibacterial disc diffusion assays with *Staphylococcus aureus* and *Fusobacterium ulcerans*, MMP-9 enzyme inhibition and dermal fibroblast stimulation assays were carried out on plant saps and aqueous extracts of plant material. LC-MS was used to identify known plant metabolites.

Results: The ethnobotanical survey identified sixteen species that were used to treat tropical ulcers, all of which were applied topically. A subset of twelve species were investigated further *in vitro*. Four species produced zones of inhibition with *S. aureus*, all 12 species provided low level inhibition of MMP-9 and 8 species stimulated dermal fibroblast proliferation, although cytotoxicity occurred at higher concentrations. The extract of *Homalium foetidum* Benth. inhibited *S. aureus* and MMP-9 while at lower sub-cytotoxic concentrations stimulated fibroblast proliferation. Trans-3-O-p-coumaroylquinic acid cis-3-O-p-coumaroylquinic acid were detected in the aqueous extract of *H. foetidum*.

Conclusions: Topical application of plant saps to wounds results in very high localised concentrations of plant metabolites which is likely to result in inhibition of MMP proteases. *H. foetidum* is a candidate plant for tropical ulcer treatment in remote areas.

1. Introduction

The tropical ulcer is an extremely painful and debilitating bacterial infection (Lupi et al., 2006). It commonly affects children and adolescents and presents as a rapidly growing ulcer of the lower leg (Adriaans and Drasar, 1987). Treatment options include skin grafting, antibiotics such as metronidazole, and topical antiseptics such as gentian violet (Singal and Grover, 2015). Evidence suggests that treating tropical ulcers may place a considerable burden on government aid posts in Papua New Guinea with up to a third of their time

Abreviations: MMP-9, matrix metalloproteinase-nine

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[1] Ethnobotanical field work and in vitro assays.
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[5] Microbiology
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and half their budgets spent treating the condition (Morris et al., 1989). For remote populations in Papua New Guinea, treatment options are extremely limited. It is not practical for the government to deploy basic healthcare infrastructure across remote areas which are not even accessible by light aircraft. There is therefore a strong rationale for early treatment of small bacterial skin infections with locally available antibacterial plants rather than late treatment of chronic tropical ulcers in a hard to reach clinic. Furthermore, in Papua New Guinea, for populations that have access to healthcare, antibiotics are widely available and are even applied topically to tropical ulcers, a practice which would be expected to contribute to the development of antibiotic resistance. Using antibacterial plants as first line topical antiseptics, may help reduce this risk.

Tropical ulcers start as infected scratches or insect bites but may become several centimetres in diameter within a couple of weeks (Lupi et al., 2006). The ulcers have a well-defined undermined edge and a characteristic foul smelling slough overlaying a soft and easily bleeding base of inflamed tissue (Adriaans and Drasar, 1987; Falkler et al., 1989). The aetiology of the ulcer remains unclear; attempts to isolate the causative pathogen(s) have yielded *Treponema spp*., fusiform bacteria such as *Fusobacterium ulcerans*, *Staphylococcus aureus, Corynebacterium haemolyticum* and more recently *Haemophilus ducreyi* suggesting some or all of these organisms are involved in the pathogenesis (Adriaans and Shah, 1988; Bowness et al., 1984; Lupi et al., 2006; Mitja et al., 2014).

In the present study we present an ethnobotanical survey of plants used to treat tropical ulcers by a little known semi-nomadic population who roam deep into Whiteman Range in the mountainous interior of West New Britain Province (Fig. 1). They refer to themselves as Apsokok and have apparently broken away from larger settled Apsokok communities that live in established villages on either side of the Whiteman Range. This population of less than a fifty people, consists of a small number of family groups each living in temporary open sided shelters in widely dispersed forest clearings 100 m in diameter. The nomadic Apsokok are able to recall a time before the Second World War when they lived in forest on the South Side of the Whiteman Range; startled by the appearance of wartime aircraft they moved deeper into the interior of the island. In the 1970s most family groups settled at the village of Ishmin on the Kulu River enabling them to find employment in the surrounding oil palm plantations. The remaining family groups who have opted to continue a semi-nomadic lifestyle inland, periodically visit their relatives in Ishmin to acquire essential supplies such as salt, and metal implements. For this small, hard to access population, it would be useful to identify which plant species could be used in the place of conventional first line treatments.

2. Materials and methods

2.1. Ethnobotanical data collection

Consent for this study was obtained from local participants and the government of Papua New Guinea prior to commencement. In May 2014, informal interviews were carried out with a key informant from one of the semi-nomadic families in a forest clearing at S 5° 39.69 E 150° 0.14 and this information was used to provide a provisional list of medicinal plants. In March 2016 more extensive interviews were carried out with several informants living downriver in the small settlement of Milawak S 5° 39.37 E 150° 0.89 and two other small clearings nearby. This allowed the names of tropical ulcer plant medicines to be expanded from information recorded in 2014 and in most cases corroborated through separate interviews with informants in these new locations. All interviews were conducted in Neo-Melanesian (Tok Pisin) language. As described previously, care was taken not to overly rely on data from any single informant (Etkin, 1993).

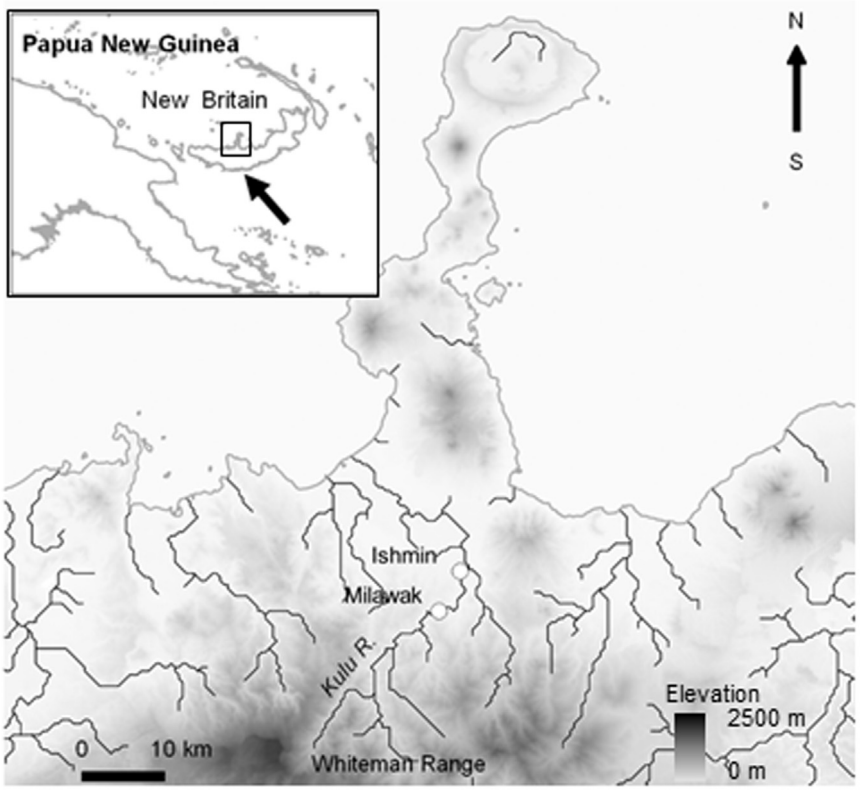

Fig. 1. Location of Ishmin village and the temporary settlement of Milawak in West New Britain Province, Papua New Guinea. The ethnobotanical survey was carried out in small rainforest clearings within a 2 km radius of Milawak. Rainforest clearings can be observed on satellite imagery along the upper branches of the Kulu River and these are consistent with geographical descriptions of temporary Apsokhok camps given by informants.