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Chaga (*Inonotus obliquus*): a medical marvel but a conservation dilemma?

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Fungi have a rich history of medicinal use within many cultures. In most cases it is the fruiting body that is harvested and appreciated. Historical use of the species *Inonotus obliquus* is different, in that it is a conk-like structure of sterile mycelial mass formed in a pre-sporulation phase, that is utilized. Analysis of 7,516 occurrence records shows a largely circumboreal distribution and further investigation reveals an affinity for tree hosts in the *Betula* genus. The medicinal benefits of this sterile-mass, known as 'Chaga' have recently been proven with potent anticancer, antioxidation, anti-inflammatory and antidiabetic activity having been reported. However, the academic interest in this species has fuelled a boom in the commercial exploitation of a product that is almost exclusively harvested from the wild. The huge harvesting of this organism in its pre-reproductive (pre-sporulation) phase rises significant issues. The medicinal properties of this species are discussed along with the conservational concern. Possible alternatives, such as cultivation are discussed along with a call for urgent educational and legislative approaches to protect a species with a rich pattern of use by cultures both contemporary and historically.

Keywords: medicinal mushrooms, traditional medicine, secondary metabolites, conservation, cultivation.

The species *Inonotus obliquus,* is a wood-rot fungus of living trees. The fungus enters through wounds within the tree and from there may develop for an estimated 10–80+ years causing decay and forming a sterile mycelial mass (Lee et al. 2008). The sexual stage begins once the tree is killed and fruiting bodies are formed beneath the bark. However, it is the pre-sporulating sterile mycelia mass that is most often observed and occurs as a conk-like structure or a black growth on the exterior of the tree (see Fig. 1). The exact role of this sterile conk is still unknown and although it contains chlamydospores, infection is thought to arise from basidiospores produced by the fruiting bodies (Lee et al. 2008). Collecting 7,516 geotagged records from the Global Biodiversity Database (www.GBIF.com, accessed 11am GMT 31st of January 2020), representing ten separate herbarium and occurrence databases, it is clear that this species has a largely circumboreal distribution (see Fig. 1). However, whether this distribution of occurrence records represents one species with a broad geographic range or multiple related species with some anatomical similarities, remains to be elucidated. The sterile conks are referred to by many names but the most common is 'chaga' and they have a long history of use by local populations, often the hard woody mass is boiled to make a tea, which is drunk to treat a range of conditions, including cancers, viral and bacterial infections, and gastro-intestinal disorders (Spinosa 2006). For example, the Khanty people of western Siberia use this species to treat heart and liver disease as well as for general internal cleaning (Saar 1991). In recent years this species has enjoyed a renaissance with a wealth of papers now published, dedicated to its medicinal use and health benefits. These range from an antioxidant effect (Cui et al. 2005) to immune-stimulating resulting in dramatic anti-cancer properties (Kim et al. 2006). Indeed, *I. obliquus* is now one of the most intensely researched of all medicinal fungi. Here, alongside a review of the current understanding of the medicinal properties of this species, we discuss the unfolding conservational conundrum arising from overharvesting and suggest ways in which this may be mitigated.

Purported medicinal properties

Chaga has been found to contain a host of pharmacologically active compounds that beneficially

Fig. 1. The sterile conk-like mass of *Inonotus obliquus* (left), known as 'Chaga', growing on *Betula pendula (*phot. Paul W. Thomas, near Pitlochry, Scotland, UK) and the circumboreal distribution of Chaga from 7,516 geotagged records from the Global Biodiversity Information Facility https://www.gbif.org/occurrence/map (right).

affect human health (Zjawiony 2004, De Silva et al. 2013). The biological activity of *I. obliquus* is mainly due to the presence of several polysaccharides, constituting the following sugars: rhamnose, arabinose, xylose, mannose, glucose, and galactose (Hu et al. 2017). Additionally, in the last decade, several studies have reported biological activities of *I. obliquus* such as anticancer, antioxidation, anti-inflammatory, antidiabetic and enhancement of immunity (Choi et al. 2010). Remarkably, a number of studies demonstrates little or no side effects during use in disease treatment (Wasser 2002, Choi et al. 2010, Elkhateeb et al. 2019). The biological activities of *I. obliquus* are discussed below.

Antioxidant activity

Various compounds extracted from Chaga have been reported to exhibit an antioxidant activity. Nakajima et al. (2007) illustrated superiority of the antioxidant activity (both superoxide and hydroxyl radicals scavenging activities) of a hot water extract of Chaga in comparison with those of other medicinal fungi namely *Agaricus blazei* mycelia, *Ganoderma lucidum* and *Phellinus linteus*. Further determination of the antioxidant potential of the isolated fruiting body (spore-generating mass) and Sclerotium (Chaga) revealed that an 80 % methanolic extract of the fruiting body had a higher potential than that of Chaga decoction.

Antidiabetic

Chaga extracts (CE) function as an antidiabetic through the lowering of blood glucose levels. Polysaccharides, which represent one of the main components of CE are capable of inhibiting alpha-glucosidase, a carbohydrate-hydrolysing enzyme. Hence, CE may act as a hypoglycemic agent by retarding glucose absorption in digestive organs and thus preventing hyperglycemia following meals (Chen et al. 2010, Lu et al. 2010, Wang et al. 2017). Sun et al. (2008) and Xu et al. (2010), reported that polysaccharides of *I. obliquus* are capable of reducing glucose, triglycerides, fatty acids, and cholesterol levels in blood.

Anti-inflammatory activity

Causes of inflammation can range from wounds, burns, infections, stress, free radicals, radiation and allergies, to immune system disorders. Drugs reducing inflammation are called anti-inflammatories. Van et al. (2009) tested several different types of extractions from Chaga, for their ability to reduce inflammation. All of those tested significantly inhibited inflammation, including a water-based polysaccharide extract and an ethanol-based extract. Kim et al. (2007) and Choi et al. (2010) found similar results with ethanol extracts.

Anticancer activity

The anticancer activity of CE is perhaps the most widely reported health benefit and that which has received the most interest. The cytotoxic and/or apoptotic effects of CE have been demonstrated in numerous *in vitro* studies in cancer cell lines, including the human colon cancer cells and the human hepatoma HepG2 cells (Youn et al. 2008). Polysaccharides isolated from *I. obliquus* sclerotium have a direct antitumor effect due to protein synthesis inhibition in tumour cells. Also, polysaccharides derived from the mycelium of *I. obliquus* function by activating the immune system. Due to the limited toxicity of these substances, both extracts as well as isolated and purified chemicals may be a good alternative to current chemotherapy and have potential for a role in cancer prevention (Staniszewska et al. 2017).

Heteropolysaccharides and homoglucans isolated from the sterile conk as well as endopolysaccharides present in the mycelium differ in the mechanism of antitumor activity; polysaccharides from sterile conks act directly on the tumour cells and endo-polysaccharides act indirectly by activating the immune system in a way similar to bacterial lipopolysaccharide (Kim et al. 2006). The triterpenoid inotodiol showed the strongest anti-proliferative effect on breast cancer Walker 256 cell line (Nakata et al. 2009). Kang et al. (2015) reported that ergosterol peroxide acts as an antiproliferative agent and also inhibits the colony formation ability of tumour cells HCT116, HT-29, SW620 and DLD-1 cell lines of colon. The Ergosterol peroxide from *I. obliquus* exhibits anticancer activity by down-regulation of the β-catenin pathway in colorectal cancer and it shows that it down-regulated β-catenin signalling; this proves that *I. obliquus* can be developed as a promising medicine to treat colon cancer (Kang et al. 2015). Nakajima et al. (2009) show that phenolic compounds of methanolic *I. obliquus* extract demonstrate a target toxicity against several lines of cancer cells and the absence of cytotoxic effects against normal cells.

Summary of identified medicinal compounds and their action

Over 200 compounds have been extracted and identified from *I. obliquus* (Rogers 2011). These compounds belong to various chemical groups such as lipids, carbohydrates, polyphenols, and terpenes. The list of compounds extracted from *I. obliquus* includes but are not limited to β-sitosterol, fecosterol, episterol, β-glucans, xylogalactoglucose, phelligridins D, 3,4-dihydroxybenzalacetone, inonoblins A, vanillic acid, syringic acid, ferulic acid, trametenolic acid, p-hydroxybenzoic acid, foscoperianol D. Some of the biologically active compounds extracted from *I. obliquus* actually originate from the host tree itself and these include betulin, betulinic acid and such compounds are absent in cultivated strains grown in the laboratory. Some of the biologically active compounds extracted from *I. obliquus* are listed in Table 1.

Tab. 1. General compounds extracted from *I. obliquus* and their biological activities.

Compound	Chemical group	Biological activity	References
Betulin	Terpenes	Antibacterial, protective effects against cadmium induced cytotoxicity	Oh et al. (2006), Géry et al. (2018)
Betulinic acid	Terpenes	Antibacterial, anti-malarial, anti-inflammatory, anti-HIV activities and cytotoxicity against a variety of tumor cell lines	Yogeeswari & Sriram (2005), Kvasnica et al. (2005), Crevelin et al. (2006), Moghaddam et al. (2012)
Inotodiol	Triterpenes	Anticancer, inhibits cell proliferation	Nomura et al. (2008), Zhong et al. (2011), Géry et al. (2018)
Lupeol	Triterpenes	Anti-inflammatory and anti-cancer	Saleem (2009)
Caffeic acid	Polyphenol	Anti-cancer, inhibits cell proliferation	Kuriyama et al. (2013)
Trametenolic acid	Sterol	Anti-inflammatory	Ma et al. (2013)
Melanin	Melanins	Antioxidant, protect DNA from damage	Babitskaya et al. (2000)
3,4-dihydroxybenzalacetone	Polyphenol	Anticancer, regulates expression of genes promoting, anti-apoptosis, and cell proliferation.	Sung et al. (2008), Kuriyama et al. (2013)
Glucans	Carbohydrates	Immune modulator	Lindequist et al. (2005)
Ergosterol peroxide	Sterol	Anticancer, antimicrobial, immunosuppressive	Merdivan & Lindequist (2017)
Inonoblin A	Polyphenol	Antioxidant	Lee et al. (2007)
Phelligridin D	Polyphenol	Antioxidant, anti-inflammatory	Lee et al. (2007)

Figs. 2–5. Different products containing Chaga. **2.** *Inonotus obliquus* tablets supplement (https://www.vitaminshoppe.com), **3.** *I. obliquus* supplement capsules (www.mycomedica.eu), **4.** *I. obliquus* fermented (www.kz.iherb.com), **5.** *I. obliquus* extract (www. emersonecologics.com).

Commercial exploitation and conservation

Commercial exploitation of Chaga-based products

The intense medicinal interest has resulted in a rise in the awareness of Chaga within the wider population. For example, a Google Trend analysis reveals that the search-term 'Chaga' has increased in popularity, four-fold in the last 10 years (to 2019). Consequently, Chaga-based products are now widely available, primarily as dried and powdered wild-harvested sterile conk. A recent search for 'Chaga health products' returned 1,390,000 hits on google.com (accessed 11am BST 1st of October 2019) and Amazon.com currently list over 4,000 products with the keyword 'Chaga' (accessed 11.30am BST 1st of October 2019). The wide range of products, from oral capsules to powdered 'tea' are presented as having some form of heath or nutritional benefit and products derived from mycelial growth are considered inferior to those of wild-harvested sterile conk (Kukulyanskaya et al. 2002). Examples of such products are displayed in Figs 2–5.

A growing conservational worry and the potential role of cultivation

Intense interest in, and the resulting harvest of, natural products for commercial exploitation can have a serious ecological impact and this has been observed in other medicinal fungi such as *Cordyceps* (Stone 2015). The concern is that *I. obliquus* may also be vulnerable to commercial harvesting practices. Although one previous attempt has been made to assess the sustainability of Chaga harvesting (Pilz 2004), the report is over 10 years old and precedes the current unprecedented demand whilst also ignoring the unknown impact of harvesting the sterile conk on the full life cycle of *I. obliquus*. Worryingly, the rising interest in Chaga has not resulted in any further attempts to assess either the direct or indirect ecological impact of increased harvesting pressure.

The slow growing nature of *I. obliquus,* taking many decades to form reproductive structures and combined with the ease of sterile conk harvest at a pre-sporulation stage, puts this species at theoretical threat of over collection. Importantly, the sterile conk forms perennially whereas the spore-bearing portion only occurs once in the lifecycle, as the tree (or part thereof) dies (Lee et al. 2008). Indeed, we are now in a situation where we are commercially harvesting large quantities of an organism of which we know very little about, with disregard for any ecological impact on the target species or those that may be interdependent.

One obvious remedy is to develop Chaga cultivation. Although *I. obliquus* is easily cultured, the products derived from mycelial growth are considered inferior and do not contain the full suite of bioactive compounds found within wild-harvested sterile conk (Kukulyanskaya et al. 2002). Therefore, a cultivation method is needed that would allow harvesting of the sterile conk mass and this has previously been reported (Silvan & Sarjala 2017).

Silvan & Sarjala (2017) inoculated live and mature trees with mycelium that had been grown in culture and after 3 years harvestable Chaga had been produced. Host specificity should be taken into account in any cultivation attempt and although this species is often found with trees in the *Betula* genus, there are other options. For example, using the Mycology Collections data Portal (https://mycoportal.org, accessed 11am GMT 31st of January 2020), a detailed database of records from across North America, information can be found on host tree frequency. Analysing 599 records, we found 66 contained information about the tree host. Of these, 59 (89.4 %) were in the *Betula* genus, three (4.5 %) were in *Quercus*, three (4.5 %) were for the species *Ostrya virginiana* and one (1.5 %) for *Acer rubrum* (see Fig. 6). These are records from North America only and there may be other potential hosts, including species from other continents. However, cultivation by inoculating live and mature trees may have other unintended consequences. Firstly, this method is dependent upon mature trees and so it would involve modification of existing ecosystems. Secondly,

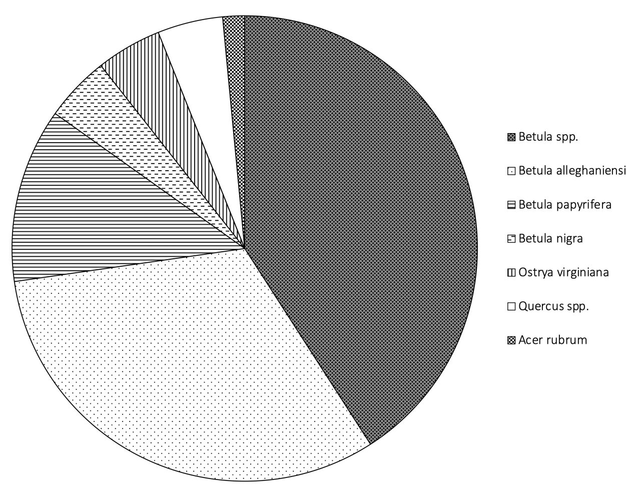

Fig. 6. Host tree records at genus or species level for entries of *I. obliquus* in the Mycology Collections Data Portal (https://mycoportal.org). The genus *Betula*, in total, accounts for 89.4 % of records.

standard practices that would be used to aid cultivation, such as strain selection to develop rapid maturation and aggressive growth, may pose another unintended ecological threat. Releasing such an enhanced strain of this parasitic fungus, optimised to rapidly infect mature standing trees, into the environment runs the risk of threatening delicate woodland habitats through rapid tree loss. Instead, perhaps, cultivation efforts should focus on novel indoor practices to produce sterile conks. Such methods are commonly utilized for other edible and medicinal wood-rotting fungi (Stamets 2011). This way, strain selection would focus on traits that benefit indoor cultivation on substrates other than mature living trees. Further, developing systems to produce sterile conks rather than mycelial extracts may lead to better acceptance in the marketplace of 'cultivated' products.

A call for action

An understanding as to the threat posed by overharvesting of this species is urgently needed. In 2004 significant harvesting pressure was already noted (Pilz 2004) and no attempt has been made since then to investigate the impact on wild populations. In addition to advances in cultivation a multipronged approach is now needed to prevent damage to wild population of *I. obliquus* and interdependent species. Firstly, an education programme within areas where there is largescale and systematic harvesting, would be beneficial to highlight the unique lifecycle of this species and its role within fragile habitats. Secondly, far more research is essential to understand the current distribution of *I. obliquus*, the impact of Chaga harvesting on this species' lifecycle and any unintended secondary consequences of harvesting practices. Thirdly, legislative support is necessary for the protection of *I. obliquus* until such time as the impact of systematic and largescale harvesting can be assessed. However, this final point is not a small task considering the geographic spread and consequently the numerous differently governed regions in which this species occurs. Nevertheless, urgent action may be necessary. Harvesting during a pre-sporulation phase and the long lifecycle combined with our lack of knowledge means that if we don't act soon, there is the potential for significant damage to be done.

Conclusion

Arising as a sterile mycelial mass on the trunk of its host tree and with a circumboreal distribution, Chaga has a rich history of medicinal use by local populations. Recent investigations have confirmed the medicinal properties and prevalence of polyphenolic composites of not just Chaga but also the mycelium and fruiting bodies of *I. obliquus*. Extracts from *I. obliquus* do indeed show much potential with significant properties that may have been appreciated historically, including: immune boosting, anti-inflammatory, antidiabetic and antibacterial. However, it is the anticancer properties that are currently receiving the most interest with the glucan and triterpenoid profile presenting the use of *I. obliquus* in some cases as a direct antitumor agent. Clearly, further research and clinical trials are needed to explore these medicinal properties more fully.

The recent medicinal interest in *I. obliquus* has, however, come at a cost to this organism. With over 4,000 products listed on Amazon alone, the scale of the commercial exploitation is evident. Chaga products are almost exclusively produced from wild-harvested pre-sporulation mycelial mass. The mass harvesting of this organism, in its pre-reproductive stage rises serious concerns for the survival of the species. Where harvesting pressure has been observed elsewhere, such as with *Cordyceps* spp. there has been a significant deleterious impact on the distribution and size of the population. The relatively long life-cycle of *I. obliquus* increases this species vulnerability.

Conservational action is now needed, and we suggest a multipronged approach of further research, an education programme within the harvesting areas, legislative support and a move towards more sustainable approaches such as cultivation and development of products based on the cultivated mycelium of this species rather than its wild-harvested mycelial mass. By raising awareness and international collaboration, we may be able to mitigate damage to populations of *I. obliquus* and interdependent species.

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