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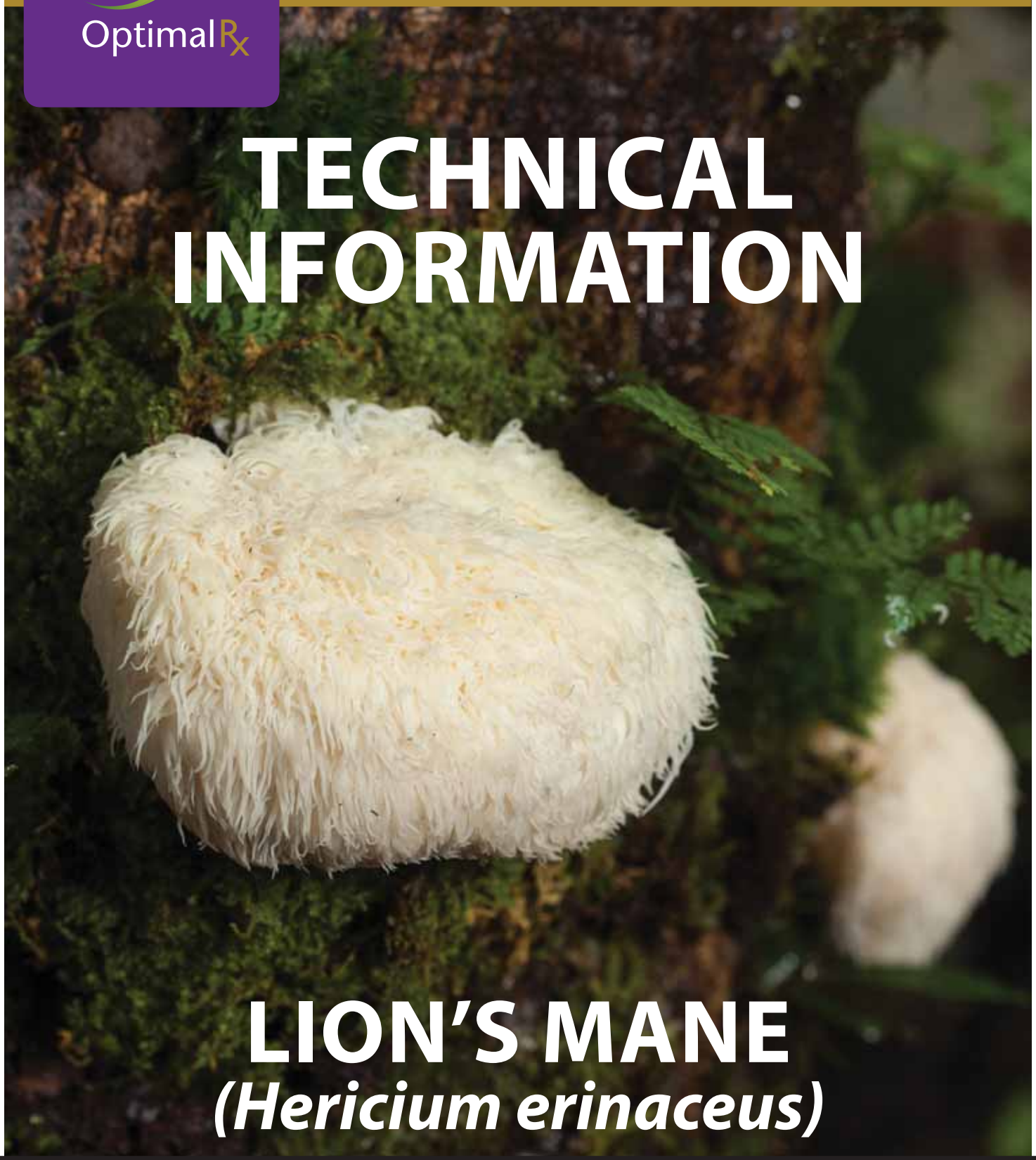
TECHNICAL INFORMATION



LION'S MANE
(Hericium erinaceus)

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Botanical Name:
Hericium erinaceus
Common Name:
Lion's Mane
Botanical Family:
Hericiaceae
Part Used:
Fruiting body
Dosage:
20ml to 50ml per week of a 1:2 liquid extract

Common Names:
Lion's Mane, Monkey's Head, Monkey's Mushroom, Bear's Head, Hedgehog Fungus, Hedgehog Mushroom, Bearded Hedgehog, Hog's Head Fungus, Pom Pom Blanc, Pom Pom, White Beard, Bearded Tooth, Houtou (Chinese), Shishigashira (Chinese), Yamabushitake (Japanese), Igel-Stachelbart (German)

Actions:
- Anti-ageing
- Antibacterial
- Anti-cancer
- Antidiabetic
- Anti-fatigue
- Anti-inflammatory
- Antioxidant
- Cardioprotective
- Gastroprotective
- Hepatoprotective
- Immunomodulating
- Neuroprotective
- Nootropic

Indications:
- Alzheimer's disease
- Bacterial infections
- Cancer adjunct
- Cognitive decline
- Dementia
- Diabetes
- Diabetic neuropathy
- Dyslipidaemia
- Fatigue
- Gastric ulcer prevention
- Gastritis
- Hepatic disease
- Inflammatory disorders
- Metabolic syndrome
- Neurodegenerative diseases
- Wound healing (topical application)

Traditional Use:

Lion's Mane *(Hericium erinaceus)* is a wood-rotting fungus belonging to the family Hericiaceae; its major fruiting body is fleshy and semi-spherical. When the fungus is young the flesh is white in colour and as it ages it becomes a yellowish-brown, once this colour change occurs the quality of the mature mushroom decreases[1]. Lion's Mane grows slowly in pairs and inhabits high on living beech or oak trunks in wild forests and its growth is greatly influenced by environmental conditions[1].

Lion's Mane is an important medicinal mushroom that has been used since ancient times in East Asia to treat neurasthenia and general debility[2]. It is commonly known as "Houtou" or "Shishigashira" in Traditional Chinese Medicine (TCM) and "Yamabushitake" (meaning "mountain priest") in traditional Japanese medicine[2]. Many of the mushroom's names are related to its conspicuous macromorphology. For instance, the Chinese name Houtou translates to "monkey head" and the scientific nomenclature *erinaceus* literally means "hedgehog" in Latin, attempting to describe the appearance of the fungus[2].

Lion's Mane is commonly prescribed in TCM due to its overall benefit on human health. It is also utilised as an edible mushroom and often seen as a delicacy in Asian countries[3]. Recently, Lion's Mane has been investigated for its profound nootropic and neuroprotective activities.

Phytochemistry:

Lion's Mane fruiting body and mycelia contain an exceptionally large amount of structurally different and potentially bioactive constituents, including polysaccharides, meroterpenoids (i.e. hericenones), cyathane diterpenoids (i.e. erinacines), steroids, alkaloids and lactones[2,4,5].

Particularly hericenones and erinacines have been found to stimulate nerve growth factor synthesis and are thought to be responsible for much of the mushroom's neuroprotective and nootropic activities[2].

Research:

Cardiovascular System

Cardioprotective:

Although clinical studies on humans are not yet available, the available preliminary research indicates that Lion's Mane may be utilised to prevent cardiovascular diseases[2].

Several preclinical studies have established that Lion's Mane extracts exhibit significant antihyperlipidaemic effects in diabetic rat models[6,7,8].

Lion's Mane has also demonstrated an in vitro inhibitory effect on low-density lipoprotein (LDL) oxidation as well as on the activity of the cholesterol biosynthetic key enzyme 3-hydroxy-3-methyl glutaryl coenzyme A (HMG Co-A) reductase activity[9]. This shows therapeutic potential for the prevention of oxidative stress-mediated vascular diseases, such as atherosclerosis.

Interestingly, an isolated constituent from Lion's Mane, hericenone B, exhibited strong antiplatelet aggregation in rabbit and human platelet cells, by a mechanism that blocks collagen-induced platelet aggregation through the inhibition of arachidonic acid release in integrin α2/β1 signalling[10]. This in vitro data may indicate that Lion's Mane has potential to be utilised to prevent cardiovascular disease and stroke.

A preliminary in vitro investigation has also found that Lion's Mane extract displayed some angiotensin converting enzyme (ACE) inhibitory effects, an indicator of in vivo antihypertensive activity[11]. These effects however were minimal compared with *Ganoderma lucidum* (Reishi) mushroom extract evaluated in the same study[11].

Endocrine System

Antidiabetic:

The intraperitoneal administration of an aqueous extract of Lion's Mane at 100mg/kg and 200mg/kg body weight to diabetic rats for 28 days resulted in a significant decrease in serum glucose level and a significant increase in insulin level, compared to control rats[6]. Treatment with the Lion's Mane extract also attenuated serum lipid disorders, decreasing serum triglyceride (TG), total cholesterol (TC), and low density lipoprotein (LDL) levels, and increasing high density lipoprotein (HDL) level in diabetic rats. These results indicate that Lion's Mane treatment may be able to normalise the lipid profile in diabetic rat models by regulating blood glucose and insulin[6]. These findings were accompanied by increased activities in endogenous antioxidant enzymes and reduced oxidative stress parameters known to damage liver function, suggesting that the antidiabetic mechanism of Lion's Mane may involve the inhibition of reactive oxygen species (ROS).

One of the most common chronic complications of diabetes mellitus is diabetic neuropathy, which is mainly characterised by spontaneous pain and abnormal sensations such as paraesthesia, allodynia, and hyperalgaesia[12]. A large number of neuroanatomical, neurophysiological, and neurochemical mechanisms are thought to contribute to the development and maintenance of diabetic neuropathic pain and Lion's Mane has demonstrated a neuroprotective effect against neuropathic pain in diabetic animal models. Researchers reported a reduction in alloxan-induced diabetic neuropathic pain in rats following 40mg/kg oral administration of an ethanolic extract of Lion's Mane fruiting body for six weeks[12]. This effect was associated with a significant increase in the total in vivo antioxidant status (TAOS) as well as restored endogenous antioxidant enzymes[12].

Furthermore, Lion's Mane may assist with poor wound healing, another common complication of diabetes. Topical application of an aqueous extract from the fruiting bodies of Lion's Mane enhanced the acceleration of wound healing in experimentally wounded and dressed rats[13].

Anti-fatigue:

Polysaccharides extracted from Lion's Mane fruiting body were found to exhibit anti-fatigue activities in a recent in vivo study[3]. After one week of acclimatisation in this mouse model, mice were randomly divided into four groups; a control group, a low-dose Lion's Mane extract group (50mg/kg), a moderate-dose Lion's Mane extract group (100mg/kg), and a high-dose Lion's Mane extract group (200mg/kg). Mice were administered treatment orally once daily for 28 consecutive days. Following this treatment period, the mice performed a

forced swimming test until they were exhausted, then the exhausted swimming time was recorded along with biochemical parameters related to fatigue including blood lactic acid (BLA), serum urea nitrogen (SUN), tissue glycogen, superoxide dismutase (SOD), glutathione peroxidase (GPx), and malondialdehyde (MDA)[3].

Results of this investigation indicated that all tested doses of Lion's Mane polysaccharides exhibited significant anti-fatigue activity preclinically, evidenced by lowered BLA, SUN, and MDA content, and by increased tissue glycogen content and antioxidant enzyme activity. Exhausted swimming times in all Lion's Mane groups were significantly longer than in the control group ($p<0.05$), suggesting the polysaccharides were able to elevate the exercise tolerance in mice[3].

Lion's Mane may therefore contribute to the improvement of metabolic control of exercise and the activation of energy metabolism, which may ameliorate physical fatigue by increasing storage of glycogen in the liver and muscles. Furthermore, Lion's Mane may upregulate endogenous antioxidant enzyme activity, reduce lipid peroxidation, and prevent exercise-induced oxidative damage to reduce physical fatigue[3].

Gastrointestinal System

Gastroprotective:

Lion's Mane has been used regularly in TCM clinical practice, either alone or combined with other remedies, for the treatment of ulcers, inflammation and tumours of the digestive system[14,15].

Pretreatment with the freeze-dried fruiting bodies of Lion's Mane was seen to decrease gastric mucosal damage and oedema in vivo and provide cytoprotection against ethanol-induced gastric ulcers in rats[16]. The data from this animal study demonstrated that the cytoprotective effect of 500mg/kg^{-1} of Lion's Mane was comparable to omeprazole, a pharmaceutical proton pump inhibitor (PPI)[16].

Lion's Mane ethanolic extract cultivated with *Artemisia capillaris* has also been shown to relieve the gastric mucosal damage in a rat gastritis model[17].

Additionally, ethanol extracts and ethyl acetate fractions of Lion's Mane have been shown to inhibit the growth of both antibiotic-resistant and non-resistant pathogenic strains of *Helicobacter pylori* in vitro[14]. *Helicobacter pylori* is a microaerophilic, Gram-negative bacterium that thrives in the acidic environment of the stomach and is associated with an increased risk of duodenal and gastric ulcers, gastric adenocarcinoma, and gastric lymphoma[14].

Hepatobiliary System

Hepatoprotective:

Lion's Mane has been reported to possess hepatoprotective effects, which have been linked to the mushroom's antioxidant activity[3,4,6].

Three fractions of endo-polysaccharides from the mycelium of Lion's Mane, grown on tofu whey, were obtained by fractional precipitation with an ethanol gradient. The studies for evaluating the antioxidant potential and the hepatoprotective effects against carbon tetrachloride injury revealed that each of the polysaccharides had differing activities in several evaluation systems. The polysaccharide precipitated with 80% ethanol demonstrated the strongest antioxidant activity in vitro and a potent hepatoprotective effect in vivo[18].

Lion's Mane mushroom extracts have also been shown to protect infected mice against *Salmonella* Typhimurium-induced liver damage by stimulating innate immune cells[19].

Immune System

Antibacterial:

Medicinal mushrooms are known to be rich sources of secondary metabolites that possess activity against certain pathogenic microorganisms. Accordingly, Lion's Mane has been shown to be a source of a number of antimicrobial agents[2].

Various Lion's Mane extracts strongly inhibited the growth of four out of five Gram-positive bacteria (*Bacillus cereus, Bacillus subtilis, Staphylococcus aureus* ATCC 6538, and *Enterococcus faecalis* ATCC 70, but not *Staphylococcus aureus*) and five out of eight Gram-negative bacteria (*Salmonella* spp. ATCC 13076, *Salmonella* Typhimurium, *Shigella* spp., *Pseudomonas aeruginosa*, and *Plesiomonas shigelloides*, but not *Shigella flexneri* ATCC 12022, *Escherichia coli* ATCC 29552 or *Escherichia coli* strain O157) tested in an in vitro trial[15]. The strength of inhibition depended on the type of extract used; Lion's Mane fresh fruit body, freeze-dried fruit body, and mycelium effectively inhibited multiple bacteria whereas the oven-dried fruit body was less active[15].

In a separate study, a mycelium extract of Lion's Mane exhibited a minimal inhibitory concentration (MIC) with an EC50 value of 5.5µl/ml against *Staphylococcus aureus*[20].

In vitro studies have also determined that bioactive erinacines, isolated from cultured Lion's Mane, exhibited potent antibacterial activity against methicillin-resistant *Staphylococcus aureus* (MRSA)[21]. The results from these investigations indicated that the three-ring skeleton of the aglycone in the active compounds was indispensable to the anti-MRSA activity[21].

The antibacterial effect of Lion's Mane was also tested against the foodborne pathogen, *Salmonella* Typhimurium, and although the Lion's Mane extracts studied were found to be inactive against this pathogen in vitro, they were able to protect mice against lethal infection in vivo through the activation of innate macrophage immune cells[19]. Intraperitoneal administration of an ethanolic extract and a hot water extract of Lion's Mane improved liver morphology (as liver necrosis is a biomarker of in vivo salmonellosis) and life expectancy in *Salmonella* Typhimurium infected mice. The beneficial effects were paralleled by changes in several in vitro parameters measured in cultured murine macrophage cells associated with the immune system[19]. Thus in this case, researchers suggested that Lion's Mane may be able to protect the liver by stimulating innate immune cells, which then kill the *Salmonella* Typhimurium bacteria that induced the liver injury[19].

Ethanolic extracts of Lion's Mane inhibited the growth of *Helicobacter pylori* and *Staphylococcus aureus* strains in vitro, however these extracts had no effects on the growth of two *Escherichia coli* test strains[14]. The in vitro inhibitory effect of Lion's Mane extracts against *Helicobacter pylori* strains suggests antimicrobial mechanisms that do not seem to involve the immunomodulating effects observed with the mushroom's polysaccharides[14].

The anti-*Helicobacter pylori* activities of two novel polysaccharides isolated from Lion's Mane were also evaluated in vitro, and were found to effectively inhibit the bacteria both on their own and when combined with a bismuth compound[22]. Bismuth compounds have been widely used for the treatment of gastrointestinal disorders and Helicobacter pylori infection together with antibiotics. However, as bismuth toxicity can cause terrible side effects, research aims to find effective complexes that allow for lower concentrations of bismuth[22]. In this study, the Lion's Mane polysaccharides themselves demonstrated definite inhibition effects on *Helicobacter pylori*, and the combined polysaccharide and low concentration bismuth complex exerted even stronger inhibition effects on *Helicobacter pylori* (MIC = 20g/mL), which was comparable to colloidal bismuth subcitrate containing a higher content of bismuth[22].

Anticancer:

Lion's Mane and its constituents have been shown to have anticancer activities in vitro against many cancer cell lines including MCF-7 breast cancer, HeLa cervical cancer, HL-60 leukaemia, U937 human monocytic leukaemia, and HepG2 hepatoma cells[23,24,25,26,27].

Polysaccharides isolated from Lion's Mane have demonstrated antiproliferation and antioxidant activities in vitro[23]. When compared with the polysaccharides isolated from seven other species of medicinal mushrooms, Lion's Mane polysaccharides had the strongest inhibitory effect on HeLa cervical cancer cells[23].

Lion's Mane was also seen to enhance the apoptotic effect of doxorubicin in preclinical trials, acting as an enhancer to sensitise doxorubicin-mediated apoptotic signalling by reducing (FADD-like IL-1β-converting enzyme)-inhibitory protein (c-FLIP) expression via c-Jun N-terminal kinase (JNK) activation and enhancing intracellular doxorubicin accumulation via the inhibition of nuclear factor kappa B (NF-κB) activity. These findings suggest that Lion's Mane may have the potential to provide synergistic therapeutic effects against drug-resistant human hepatocellular carcinoma[27].

Anti-inflammatory:

Molecular targets of inflammation include cytokines such as interleukins (IL) and tumour necrosis factor alpha (TNF-α), chemokines, cyclooxygenase-2 (COX-2), prostaglandins, inducible nitric oxide synthase (iNOS), nitric oxide (NO) and so on[1]. Mechanistic investigations have determined that Lion's Mane is able to influence many of these inflammatory markers, regulating and modulating the inflammatory process[1,28].

A Lion's Mane aqueous extract was seen to induce IL-1β expression in murine macrophages at a transcriptional level by enhancing the activation of transcription factors, NF-κB, NF-IL6, and activator protein 1 (AP-1)[29]. Lion's Mane aqueous extract also induced iNOS gene expression followed by NO production in macrophages via enhancing the activation of NF-κB[30].

Findings from a recent in vitro study indicate the possibility that Lion's Mane exerts anti-inflammatory effects on macrophages through the inhibition of toll-like receptor 4 (TLR4)-JNK signalling and prevents or ameliorates adipose tissue inflammation associated with obesity[31].

Lion's Mane extract has also provided a protective effect against LPS-induced inflammation by suppressing the generation of excessive active pro-inflammatory mediators, including NO, ROS, prostaglandin E2, IL-1β, and TNF-α[28,31,32,33].

Antioxidant:

An in vitro study investigated the antioxidant capacity of methanolic Lion's Mane extracts, establishing that the mycelium extract tested contained the highest total phenolic content (polyphenols are multifunctional antioxidants that act as reducing agents, hydrogen donating antioxidants and singlet oxygen quenchers) and the highest ferric reducing antioxidant power (FRAP), whereas the fresh fruit body extract showed the most potent l,l-diphenyl-2-picrylhydrazyl (DPPH) radical scavenging activity[15]. All extracts tested demonstrated antioxidant activities.

A recent preclinical study evaluating the antioxidant activity of polysaccharides obtained from eight different medicinal mushroom species found that all the extracts demonstrated significant antioxidant capacity however the polysaccharides from Lion's Mane exhibited the highest DPPH radical scavenging activity out of all the mushrooms tested[23].

An aqueous extract of Lion's Mane was able to restore the antioxidant status in treated diabetic rats, increasing the activities of catalase (CAT), SOD, and GPx, increasing glutathione (GSH) level, and reducing the MDA level in the rat's liver tissue significantly[6].

Immunomodulating:

Preclinical studies have reported that Lion's Mane and associated polysaccharides are able to modulate the immune system in various animals and in dendritic cell cultures[4].

Dendritic cells are antigen-presenting cells that act as mediators of peripheral immune tolerance and help maintain immune homeostasis[4]. An evaluation of several biomarkers associated with the immunomodulatory effects of polysaccharides isolated from Lion's Mane showed that these constituents stimulated the maturation of rat dendritic cells significantly, induced dendritic cell activation and modulated the T helper (Th)1 immune response[34]. Researchers suggested that these findings elucidate the potential value of polysaccharides as immunopotentiating agents.

In a separate study, all 21 fractions of polysaccharides extracted from Lion's Mane fruiting body were able to significantly stimulate macrophages to release NO and demonstrated effective immune activity in vitro at 50μg/ml[35].

The activity of polysaccharides isolated from the cultured broth of two *Hericium* spp. was compared and found that both species had significant anti-artificial pulmonary metastatic tumour effects in mice ($p<0.05$). Additionally, the polysaccharide from *Hericium erinaceus* (Lion's Mane) was more effective than that from *Hericium laciniatum*. However, constituents from both species increased T cells in the mouse model, indicated by higher numbers of CD4+ cells and macrophages in the test groups compared to controls[36]. This data indicates that potential anti-tumour activity of Lion's Mane might be associated with the immunoenhancing effects of the

polysaccharides.

In vivo studies have demonstrated that Lion's Mane is able to improve the innate immune response and disease resistance in animals by modulating nonspecific defence mechanisms against pathogens and improving mortality rates[37,38,39].

Nervous System

Depression & Anxiety:

A randomised, double-blind, placebo-controlled clinical trial investigated the use of Lion's Mane in the reduction of depression and anxiety[40]. Thirty females between the ages 41 years and 46 years were enrolled into the study where the researchers assessed the clinical effects of Lion's Mane on symptoms of menopause, depression, sleep quality and indefinite complaints. The participants were randomised to receive either 2g per day of Lion's Mane extract or placebo for a period of four weeks. At completion of the trial the participants ingesting Lion's Mane had a reduction in depression and anxiety symptoms, particularly in the symptoms of "frustration" and "palpitations"[40]. This study demonstrated that Lion's Mane reduced depression and anxiety in participants, while increasing cognition and the ability to concentrate.

Neuroprotective:

There are several possible mechanisms that contribute to Lion's Mane neuroprotective activities, such as its antioxidant and anti-inflammatory properties, however the precise protective mechanisms remain unclear. Animal studies have shown extracts of Lion's Mane to inhibit neurological insults in ischaemic stroke models, thereby protecting neurons from death due to ischaemic injury[41]. Part of this protective activity was due to an increase in free radical scavenging and a reduction in iNOS expression.

In many types of neurodegeneration, neuronal cell death is induced by endoplasmic reticulum (ER) stress and therefore interventions that attenuate this may provide significant neuroprotection. The constituent dilinoleoyl-phosphatidylethanolamine (DLPE) was a molecule isolated from the fruiting body of Lion's Mane and found to be effective at reducing ER stress-dependent cell death in mouse neuroblastoma cells[42].

In animal models of Alzheimer's disease, Lion's Mane attenuated the cognitive dysfunction (prevented impairments of spatial short-term and visual recognition memory) induced by β-amyloid administration, further suggesting that this phytomedicine may be useful in the treatment of cognitive decline and dementia[43].

A randomised, double-blind, parallel-group, placebo-controlled clinical trial performed on 30 Japanese men and women investigated the efficacy of oral administration of Lion's Mane for improving cognitive functioning[44]. The participants were aged between 50 years to 80 years and diagnosed with mild cognitive impairment. They were randomised to receive either Lion's Mane (1g taken three times per day) or placebo for a period of 16 weeks. At weeks eight, 12, and 16 the Lion's Mane group showed significantly increased scores on the cognitive function scale compared with the placebo group. However, at four weeks post completion of the trial the scores decreased significantly, indicating that this phytomedicine enhances cognitive function while it is being administered however the effects are not permanent[44].

In light of the numerous diseases related to neurodegeneration, Lion's Mane deserves further clinical attention.

Nootropic:

Nerve growth factor (NGF) is the most potent growth factor for cholinergic neurons and it influences the proliferation, differentiation, survival and death of neuronal cells[43,45]. It is essential for the health of the nervous system. Alterations in NGF levels have been implicated in neurodegenerative disorders, such as Alzheimer's disease and Huntington's disease, as well as psychiatric disorders, including depression and substance abuse. Signals emanating from receptors for NGF regulate many aspects of immune defence and, as such, constitute potential targets for therapeutic intervention in neurodegenerative conditions[45].

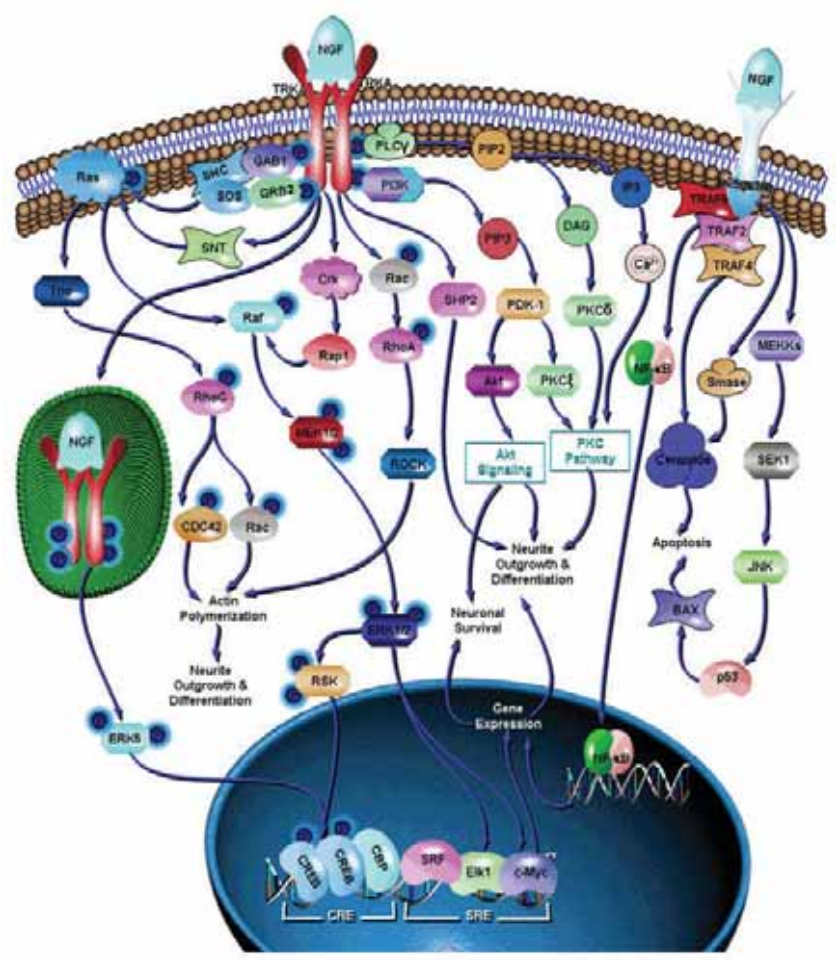

Fig 1: Nerve Growth Factor Pathway

KEY: Akt = Protein Kinase B, **BAX** = Proapoptotic Protein of the Bcl2 Family, **Ca2+** = Intracellular Calcium, **CBP** = CREB Binding Protein, **CDC42** = Cell Division Control Protein 42 Homolog GTPase Protein of Rho Family, **Ceramide** = Ceramide, **c-Myc** = c-Myc Regulator Gene, **Crk** = Class of SH2 and SH3-Containing Adaptor Proteins, **CREB** = Cyclic Adenosine Monophosphate (c-AMP) Response Element Binding Protein, **DAG** = Diacylglycerol, **Elk1** = ETS Domain-Containing Protein Elk-1, **ERK5** = Extracellular Signal-Regulated Kinase 5, **GAB1** = GRB2-Associated Binding Protein-1, **GRB2** = Growth Factor Receptor-Bound Protein-2, **IP3** = Inositol Triphosphate, **JNK** = Jun N-terminal Kinase, **MEK1/2** = Dual Specificity Mitogen-Activated Protein Kinase 1/2, **MEKKs** = MAP/ERK Kinase Kinases, **NF-κB** = Nuclear Factor-Kappa B, **NGF** = Nerve Growth Factor, **p53** = Tumour Protein p53, **PDK1** = Phosphoinositol Dependent Kinase-1, **PI3K** = Phosphatidylinositiol-3 Kinase, **PIP2** = Phosphatidylinositol 4,5-Bisphosphate, **PIP3** = Phosphatidylinositol 3,4,5-Trisphosphate, **PKC** = Protein Kinase-C, **PKCδ** = Protein Kinase-C-Delta, **PKCδ** = Protein Kinase-C- Zeta, **PLCγ** = Phospholipase-C-Gamma, **Rac** = Rac GTPase Protein of Rho Family, **Raf** = Serine/Threonine Kinase, **Rap1** = Ras-related protein 1 GTPase Activating Protein, **RAS** = GTPase Switch (or Binding) Protein, **RhoA** = RhoA GTPase Protein of Rho Family, **ROCK** = Rho-Associated Coiled-Coil-Containing Protein Kinase, **RSK** = Ribosomal S6 Kinase, **SEK1** = SAPK/ERK Kinase 1, **SHC** = SH2 Containing Protein, **SHP2** = Tyrosine Phosphatase SHP2, **Smase** = Sphingomyelin Phosphodiesterase, **SNT** = Signalling Adaptor Protein, **SOS** = A Cytosolic Protein, **SRE** = Serum Response Element, **SRF** = Serum Response Factor, **TRAF2** = TNF Receptor Associated Factor-2, **TRAF4** = TNF Receptor Associated Factor-4, **TRAF6** = TNF Receptor Associated Factor-6, **Trio** = Triple Functional Domain-PTPRF Interacting, **TRKA** = Tyrosine Kinase Receptor-A
(Image Ref: http://www.jeanpierrevarlenge.com/sciences/chimie-vivant-une-si-longue-histoire/ix-chimie-et-opium-voyages-voyages/)

Lion's Mane has been found to stimulate NGF and promote neurite outgrowth in both in vitro and in vivo studies[5,46,47,48]. NGF plays an important role in the differentiation, survival and maintenance of neuronal cells, however treatments that utilise polypeptides such as NGF are ineffective as they do not cross the blood-brain barrier[49]. Therefore, herbal medicines such as Lion's Mane that have demonstrated the ability to enhance endogenous NGF are fundamentally important in the management of cognitive decline and dementia disorders.

Furthermore, hericenone and erinacine constituents present in Lion's Mane have been studied for their ability to promote NGF biosynthesis as they are low-molecular weight compounds that may cross the blood-brain barrier[50]. These constituents are thought to be responsible for much of the mushroom's nootropic activity.

Extracts of Lion's Mane have demonstrated the ability to induce neurite outgrowth of neuronal cells, including those from the brain, spinal cord and retina, as well as promote the regeneration of peripheral nerve damage in animal models of nerve injury[46,47,49,51,52].

Lion's Mane has also been shown to enhance myelination in preclinical trials. Myelin sheaths wrap neuronal axons and play an important part in supporting and speeding up neural signals. Subsequently, damage to this structure (demyelination) leads to severe impairment of the nervous system. Extracts of Lion's Mane appear to exert neurotrophic activities and improve the myelination process without negatively impacting nerve cell growth or toxicity in both in vivo and in vitro experiments[49,53,54].

Safety:

Lion's Mane is a culinary and medicinal mushroom that has been consumed safely for hundreds of years and thus far there have been no toxicity reports resulting from long term consumption of Lion's Mane[4,55].

In two clinical studies, Lion's Mane was found to be safe with no adverse effects reported[40,44].

Safety in Pregnancy and Lactation:

Safety in pregnancy and lactation has not been established, therefore use is not recommended.

Caution:

Bleeding disorders – Theoretically, high doses of Lion's Mane may increase the risk of bleeding in certain individuals with particular bleeding disorders due to its potential anti-platelet activity[2,10].

Thrombocytopenia – Theoretically, high doses of Lion's Mane may increase the risk of bleeding in people with thrombocytopenia due to its potential anti-platelet activity[2,10].

Surgery – Theoretically, high doses of Lion's Mane might increase the risk of bleeding in certain people if used before or during surgery due to its potential anti-platelet activity[2,10]. It is recommended that the use of Lion's Mane is discontinued two weeks prior to scheduled surgery.

Interactions:

Anticoagulant / Antiplatelet medication – Theoretically, Lion's Mane may further inhibit platelet aggregation as hericenone B from the fruiting body of the mushroom has been shown to exert anti-platelet activity[2,10].

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