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REVIEW

Exploration of macrofungal wealth of West Bengal in the 21st century

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West Bengal, a phytogeographically unique state in India, is extended from Himalayas in north to Bay of Bengal in south facilitating natural growth of a variety of macrofungi. Many of these myco-resources have a long history of appreciation as functional culinary delicacies and medicine. Despite that, research on them is still lacking motivating us to convey a well-organized study on wild mushrooms not only to save our forefather's wisdom but also to promote rural economy. The endurance of past two decades has contributed 26 species new to science based on morphological analysis, anatomical features, DNA barcoding and phylogenetic position. The research was further extended to determine nutritional values of collected specimens where they appeared as potent functional food with high content of carbohydrate, protein, fiber and low level of fat. Multitudinous studies focusing on therapeutic benefits have also been carried out including antioxidant, antibacterial, antifungal, cardio-protective, anti-parasitic, anti-ulcer, hepato-protective, hypo-glycemic, anti-inflammatory, anti-neoplastic and immune-stimulation effects. Based on the outcome, pure components have been isolated from some promising taxa underlying mechanism of action. The journey is in continuation with an aim to represent mushrooms of West Bengal as promising resource for food and pharmaceutical industries.

Key words: Drug development, functional food, improved methods, novel species, pure component

INTRODUCTION

Macrofungi including mushrooms have been a part of the human culture for thousands of years with considerable interest in civilization history because of their sensory characteristics and medicinal properties (Ma *et al.,* 2018). Consequently, knowledge about their bioactive compositions and nutritional values have increased massively in the past several years defining macrofungi as potent functional food with significant content of dietary fiber and low level of fat. Moreover, high quality of proteins including most of the essential amino acids, vitamins and mineral substances are also found in Basidiomycetes (Wani *et al.,* 2010). Today researchers have explored therapeutic benefits of mushrooms as well executing about 100 different medicinal activities of which antioxidant, antimicrobial, anticancer, anti-inflammation, hepato-toxicity and immune-enhancing effects are the key properties. Indeed, prospecting for bioactive constituents from myco-resources with interesting and novel action mechanisms has now become one of the most actively pursued endeavors in drug discovery programs (Valverde *et al.,* 2015).

Such bioactive macrofungi packed with nutraceuticals are cosmopolitan in distribution although tropical environment with warm humid climate is appropriate for their natural growth. Thus, it has recently been postulated that almost 60% of the novel macrofungal species belong to tropics and in this context India harbours a treasure house of basidiomycetes being blessed with diverse agro-climatic zones (Paterson and Lima, 2014). West Bengal (21^{0}38'–27^{0}10'N latitude and 85^{0}50^0–89^{0}50'E longitude) situated at east of the subcontinent is the only state being extended from high peaks of Himalaya in northern extreme to coast of Bay of Bengal down in south, with plateau and

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Ganges delta intervening in between covering an area of approximately 88,752 km^2. As a result, the region is climatically quite distinctive as it varies from subalpine in north, sub-tropical sub-humid in central-southwestern and tropical savannah in south. Apparently, the area encompasses six agro-climatic zones such as hill (north), terai and Teesta alluvial (north), coastal alluvial (south), lateritic, red and gravely undulating (west), gangetic alluvial (west) and Vindhya alluvial (centre) regions. The state thus is a treasure house of myco-diversity nurturing natural growth of several saprophytic and mycorrhizal taxa (Pradhan *et al.,* 2012, Dutta and Acharya, 2014a).

In this backdrop, our research team is working since past 20 years to unveil West Bengal macrofungal flora by arranging regular field trips throughout the year. As expected, some of the collected specimens emerged as new to the state, country and even science; while others were identified as common bio-resource distributed in different zones. Consultancy with mycophagy elders revealed that many of these wild macrofungi have long been consumed by inhabiting people, due to traditionally known benefits. Hence to exploit these nature-derived products, we further extended our work shedding light on nutraceutical property. Investigated taxa appeared as reliable option for development of functional food and therapeutics validating their ethnic importance. In this review, an attempt has been made to summarize diversity and health beneficial property of mushrooms collected by our team from West Bengal (Figure 1) which might benefit mycologists, taxonomists, nutrationalists, biochemists, pharmacists and so forth.

Mushrooms Native to West Bengal

Mushroom collection from wild is an arduous task as most of the species exhibit patterns of diversity related largely to substratum, climate and host availability. Thus, knowledge on distributions of anticipated taxa is highly required that helps in delimiting plots representing actual habitats (Lodge *et al.,* 2004). After gathering, macrofungi are identified traditionally by their fruiting body morphologies as well as microscopic features and for that it is better to follow recognized standard keys. However, in addition to morpho-anatomical studies, DNA barcoding and phylogenetic analyses have recently been opted by mycologists to distinguish closely related taxa and validate uniqueness of specimen (Badotti *et al.,* 2017).

In this context, our research team has organized several field trips where total 3679 species have been collected till date from different regions of West Bengal. Amongst them, 1206 specimens have been workout in detail and 364 species have been identified so far. As expected, quite a few appeared as new to science based on morphological characters, anatomical features, complete internal transcribed spacer (ITS) sequences and phylogenetic placement (Table 1). While many taxa appeared as new addition to macrofungal flora of India (Acharya *et al.,* 2015c; Dutta *et al*., 2015b; Dutta *et al.,* 2015c; Dutta and Acharya*,* 2018; Dutta *et al.,* 2020b) and West Bengal (Acharya *et al.,* 2017e; Acharya *et al.,* 2017g; Tarafder *et al.,* 2017; Acharya *et al.,* 2017h; Bera *et al.,* 2018; Saha *et al.,* 2018a; Saha *et al.,* 2018b; Saha *et al.,* 2019; Das *et al.,* 2020a; Das *et al.,* 2020b; Saha *et al.,* 2020; Thapa *et al.,* 2020). After detailed characterization, collected materials were preserved following a novel protocol as described by our group (Pradhan *et al*., 2015). The specimens were finally deposited in Calcutta University Herbarium (CUH), University of Calcutta, Kolkata and The Central National Herbarium (CAL), West Bengal, India.

Nutritional Value of Mushrooms Native to West Bengal

Many researchers have documented that edible mushrooms are packed with a variety of nutraceutical compounds such as polysaccharides, dietary fibres, proteins, mineral elements, unsaturated fatty acids and vitamins. Survey revealed carbohydrate as the major component in fruiting bodies of basidiomycetes where the content ranged between 35–70% dry weight (DW) (Cheung *,* 2013). In addition, macrofungi generally consists 19–35% DW protein which is higher than many foods including milk, rice, wheat and soyabean (Wani *et al.,* 2010). In contrast, fat content is comparatively lower (1–6.7%) making mushrooms as an excellent addition to low-calorie diet (Wang *et al.,* 2014).

In this background, we have reported nutritional composition of several wild mushrooms (Table 2) where comparative analysis indicated carbohydrate (37.58–64.33 g/100 g DW) as the main component in all of the studied specimens which was at per previous reports. Alongside, protein content was also determined in appreciable quantity (15–24.6

g/100 g DW); whilst, fat was detected in lower amount (1.2–4.63 g/100 g DW) representing the studied samples as ideal dietary ingedients for health-conscious people. Moreover, fibre content was determined as well which was present in significant content (5.4–27.57 g/100g DW).

Bioactive Compounds of Mushrooms Native to West Bengal

Along with nutritional supremacy, mushrooms also contain enumerable therapeutic components that could be isolated by varying extraction parameters. As such, primary metabolites were isolated from numerous taxa using hot water, cold alkali and hot alkali systems. Chemical characterization indicated that the fractions were mainly composed of ß-glucan as evident by spectroscopy, Fourier transform infrared spectroscopy (FTIR), gas chromatography-mass spectrometry (GC-MS) and high-performance thin layer chromatography (HPTLC). Further, bioactive macromolecules have also been purified from so*me potent taxa namely Tricholoma crassum (Patra et al.,* 2012; Samanta *et al.,* 2013), *R. albonigra* (Nandi *et al.,* 2012; Nandi *et al.,* 2013; Nandi *et al.,* 2014), *Pleurotus ostreatus* (Patra *et al.,* 2013), *Entoloma lividoalbum* (Maity *et al.,* 2014a; Maity *et al.,* 2014b; Maity *et al.*, 2015), *Termitomyces clypeatus* (Pattanayak *et al.,* 2015), *Pleurotus cystidiosus* (Panda *et al.,* 2017), *Lentinus sajor-caju* (Pattanayak *et al.,* 2018), *Pleurotus djamor* (Maity *et al.*, 2019) which were found to be homo or heterogulcan with molecular mass ranging from 5.2×104 Da to 2.1×105 Da. In contrast, polysaccharide purified from *Macrolepiota dolichaula* appeared as fucogalactan with molecular weight of ~1.2×105 Da (Samanta *et al.,* 2015). On the other hand, secondary metabolites were isolated from numerous samples using ethanol, methanol, acetone and hydro-ethanol solvents. Spectroscopic and chromatographic analysis revealed that the fractions were mainly enriched in phenolic compounds where ascorbic acid and carotenoid were detected in trace. Amongst the investigated specimen, the ethanol extract from *A. hygrometricus* was further subjected to silica gel column chromatography and eluted with C6H14CHCl3 and CHCl3CH3OH yielding two novel triterpenes designated as Astrakurkurone and Astrakurkurol (Lai *et al.,* 2012). Alongside, methylene chloride-methanol mixture from *Macrocybe gigantea* was subjected to column chromatography eluted with petroleum ether-ethyl acetate gradient. The process allowed successful isolation of a new ergosteryl triterpene, Gigantenol (Chatterjee *et al.,* 2014b).

Medicinal Properties of Mushrooms Native to West Bengal

As discussed above, mushrooms are known to possess a range of medicinal properties that may provide benefits against a large number of diseases. Likewise, mushrooms of West Bengal have also been reported by our team to possess a number of therapeutic effects. Amongst these, the most common biological activities are antioxidant, anti-inflammatory, nitric oxide synthase activation, anti-ulcer, hepato-protective, cardio-protective, antimicrobial, anticancer, immuno-stimulatory and anti-diabetic properties as shown in Figure 2. The pharmacological activities of medicinal mushrooms were primarily detected by *in vitr*o assays, and in some cases followed by *in vivo* studies.

Antioxidant activity

Free radicals are oxygen-containing molecules with an uneven number of electrons which are generated inside our body as inevitable byproducts of turning food into energy. The body, long used to this relentless attack, makes many molecules that quench free radicals labeled as antioxidants (Pham-Huy *et al.,* 2008). When there are more free radicals present than can be kept in balance by antioxidants, the reactive molecules can start doing damage to fatty tissue, DNA, and proteins resulting numerous diseases. In this context, natural antioxidant supplementation with free radical scavenging activities may be relevant to maintain homeostasis (Khatua *et al.*, 2013).

In search of nature derived antioxidative compounds, we have screened the potential of numerous wild edible mushrooms using various fractions (Table 3) following modified methods as reported by our team (Khatua *et al.*, 2017b). Addressing organic extracts, aqueous-alcohol fraction exhibited the strong antioxidant property as evident by low half maximal effective concentration (EC50) values. The consequence could be justified by chemical analysis specifying presence of phenolics in significant amount. Apart from secondary metabolites, crude polysaccharides were also isolated from different studied mushrooms using various extractive solvents. Comparatively the polymers isolated by hot water process presented promising antioxidant property where crude fraction presented better potency than pure polysaccharide.

Antimicrobial activity

At present, antibiotic resistance is a serious problem being rising to high levels in an uncontrolled manner. Unique resistance mechanisms are developing and spreading worldwide, threatening treatment of various common infectious diseases. To overlap the disadvantages of existing antimicrobial drugs, other promising medicines with effective mechanism of action should be developed (Shen *et al.,* 2017).

Our research speculated that organic extracts from a number of wild edible mushrooms of West Bengal possess antibacterial effect against several human pathogens (Table 4). In addition, anti-Candidal activity has also been recorded. On the other hand, ethanol extracts from *A. hygrometricus* and *T. giganteum* significantly retarded growth of Leishmania donovani promastigotes, restricted in lipid biosynthesis and stimulated apoptosis in promastigotes. While water soluble polysaccahridic fractions of *A. hygrometricus, R. albonigra* and *Termitomyces eurhizus* were found to inhibit replication of intracellular amastigotes in macrophages (Mallick *et al.*, 2014). The isolated pure compound, Astrakurkurone induced ROS production that was found intimately associated with cell death of *L. donovani* (Lai *et al.,* 2012; Mallick *et al.,* 2015). The compound reduced parasite burden *in vivo* by inducing protective cytokines, gamma interferon and interleukin 17 (Mallick *et al.,* 2016). Alongside, ethanol extract from *G. frondosa* also showed the bioactivity through interfering in lipid biosynthesis, altering parasite morphology and inducing apoptosis in promastigotes. The fraction was also effective against intracellular amastigotes in infected macrophages and enhanced release of NO and proinflammatory cytokines. Interestingly, the fraction was found to be slightly more efficient in comparison to conventional anti-leishmanial drugs (Sultana *et al.,* 2018).

Anticancer activity

In the past decades, cancer has surpassed many other diseases to become the second leading cause of death globally. Chemotherapy is routinely used for cancer treatment; however, it still remains potentially of high risk with many side effects which are difficult to manage. On the other hand, medicinal herbs and their derivative phytocompounds are being increasingly recognized as useful complementary treatments for cancer (Desai *et al.,* 2008).

In this context, our research showed a hope in cancer chemoprevention and treatment using the bioactive components from wild edible mushrooms. For instance, administration of ethanol extract from A. hygrometricus in Ehrlich's ascites carcinoma cells halted cell cycle at sub G0/G1 phase, induced typical apoptotic morphological changes, increased expression of p53 and Bax and downregulated expression of Bcl-2 (Biswas *et al.,* 2012). Further the isolated sesquiterpenoid, Astrakurkurone, was incubated with Hep3B and HepG2 cells to determine bioactivity. The treatment selectively induced apoptosis in hepatocellular carcinoma (HCC) by disrupting mitochondrial membrane potential ($\Delta\psi m$) and inducing expression of Bax, caspases 3 and 9 (Dasgupta *et al.*, 2019). In addition, another purified triterpenoid, Astrakurkurol, exhibited remarkable anticancer potency against Hep3B cells evident by DNA fragmentation, chromatin condensation, nuclear shrinkage, membrane blebbing, inhibition of cell migration and imbalance of cell cycle distribution. Detailed analysis revealed that the incubation induced expression of Fas, caspase-8 and tBid cleavage in HCC indicating the mode of action through caspase-8-mediated intrinsic apoptotic pathway associated with inhibition at Akt and NF-κB pathway (Nandi *et al.,* 2019). Chatterjee *et al.,* (2013b) showed anticancer effect of ethanol extract from *T. giganteum* against Ehrlich's ascites carcinoma cells. The outcome was further verified in benzo[a]pyrene-induced forestomach and lung cancer in Swiss albino mice where the administration of the fraction modulated cellular redox status and pro/anti-apoptotic gene ratio (Chatterjee *et al.,* 2014, Chatterjee *et al.,* 2016). On the other hand, ß-glucan isolated from *P. djamor* inhibited cell proliferation in PA1 (Maity *et al.,* 2019). Our recent research identified two more wild edible mushrooms namely *R. alatoreticula* and *R. senecis* as novel source of potent chemopreventive drugs against HCC. The isolated organic extracts exhibited selective inhibition of Hep3B cells by augmenting intrinsic mitochondrial pathway as evident by phenotypic changes, cell cycle interference, ROS generation, $\Delta\psi m$ decrease, DNA fragmentation, change in Bax/Bcl2 ratio and activation of caspase9 (Khatua *et al.,* 2019a; Khatua *et al.,* 2021b; Khatua and Acharya, 2021a).

Table 1: List of macrofungi identified as novel species collected from different districts of West Bengal

Mushroom name	Family	Collection place	Reference
New to science			
Volvariella pusilla var. minuta K. Acharya, A.K. Dutta & P. Pradhan *var. nov.*	Pluteaceae	Santoshpur, Kolkata	Acharya *et al.,* 2012b
Marasmius midnapurensis A.K. Dutta, P. Pradhan & K. Acharya, *sp. nov.*	Marasmiaceae	Kasaphaltala, Midnapur	Dutta *et al.,* 2014
Marasmius vladimirii A.K. Dutta & K. Acharya, *sp. nov.*		Darjeeling	Crous *et al.,* 2014
Chlorophyllum pseudoglobossum J. Sarkar, A.K. Dutta & K. Acharya, *sp. nov.*	Agaricaceae	Nandigram-I block, Midnapur	Crous *et al.,* 2015
Russula kanadii A.K. Dutta & K. Acharya, *sp. nov.*	Russulaceae	Gurguripal forest, West Midnapur	Dutta *et al.,* 2015a
Marasmiellus foliiphilus A.K. Dutta, K. Acharya & Antonín, *sp. nov.*	Marasmiaceae	Gobindapur, Midnapur	Dutta *et al.,* 2015c
Russula hookarii S. Paloi, A.K. Dutta & K. Acharya, *sp. nov.*	Russulaceae	Darjeeling	Paloi *et al.,* 2015
Russula buyckii K. Acharya, A.K. Dutta & S. Paloi, *sp. nov.*		Darjeeling	Paloi *et al.,* 2016
Russula intervenosa S. Paloi, A.K. Dutta & K. Acharya, *sp. nov.*		Lodhasuli forest, Midnapur	Crous *et al.,* 2016
Marasmius luculentus A.K. Dutta, K. Acharya & Antonín, *sp. nov.*	Marasmiaceae	Berunanpukhuria North-24-Parganas	Tibpromma *et al.,* 2017
Russula alatoreticula S. Khatua, A.K. Dutta, S. Paloi, & K. Acharya, *sp. nov.*	Russulaceae	Gurguripal, West Midnapur; Shantiniketan, Birbhum; near Khairulachak, West Midnapur	Khatua *et al.,* 2017a
Russula arunii S. Paloi, A.K. Dutta & K. Acharya, *sp. nov.*		Ballygunge Science College campus, Kolkata	Crous *et al.,* 2017
Trogia benghalensis K. Acharya & A.K. Dutta, *sp. nov.*	Marasmiaceae	Central park, Kolkata	Dutta *et al.,* 2017
Clitocybula albida A.K. Dutta, K. Acharya & Antonín, *sp. nov.*	Marasmiaceae	Ballygunge Science College campus, Kolkata	Dutta *et al.,* 2018
Russula darjeelingensis S. Paloi, K. Acharya & K. Das *sp. nov.*	Russulaceae	near Love Road, Darjeeling	Paloi *et al.,* 2018
Agaricus duplocingulatoides Tarafder, A.K. Dutta & K. Acharya *sp. nov.*	Agaricaceae	Kasafaltalya, East Midnapur	Tarafder *et al.,* 2018
Lactarius benghalensis S. Paloi & K. Acharya, *sp. nov.*	Russulaceae	Near Boria forest, Jhargram	Paloi *et al.,* 2019
Hygrocybe lucida K. Acharya & A.K. Dutta *sp. nov.*	Hygrophoraceae	Basirhat, North-24-Parganas	Phookamsak *et al.,* 2019
Lactifluus midnapurensis S. Paloi & K. Acharya *sp. nov.*	Russulaceae	Kasafaltalya, Purba Midnapur	
Marasmius indojasminodorus A.K. Dutta, K. Acharya & K. Das *sp. nov.*	Marasmiaceae	Acharya Jagadish Chandra Bose Indian Botanic Garden, Howrah	
Lactarius brunneocinnamomeus Paloi, Verbeken & K. Acharya *sp. nov.*	Russulaceae	Near Lodhasuli forest, Jhargram	Paloi *et al.,* 2019
Chlorophyllum squamulosum A.K. Dutta, Soumili Bera & K. Acharya *sp. nov.*	Agaricaceae	Burdwan University campus, Burdwan	Dutta *et al.,* 2020a
Russula benghalensis S. Paloi & K. Acharya, *sp. nov.*	Russulaceae	Near Bethuradhari forest, Nadia	Yuan *et al.,* 2020
Rhodocybe brunneoaurantiaca A.K. Dutta, G. Gates & K. Acharya *sp. nov.*	Entolomataceae	Burdwan	Dutta *et al.,* 2021a
Leucoagaricus brunneodiscus A.K. Dutta & K. Acharya *sp. nov.*	Agaricaceae	Burdwan University campus, Burdwan	Dutta *et al.,* 2021b
Leucoagaricus tropicus A.K. Dutta, Stallman & K. Acharya sp. nov.		Barasat	

Immuno-stimulation activity

Stimulating immune system is considered as an important strategy to enhance body defence mechanism which would be beneficial to protect from a large number of disorders. However, the immune system fails to act as a protector under certain circumferences (Nigar and Itrat 2013). In

Table 2 : Nutritional composition of edible mushrooms collected from different places of West Bengal

Name of mushroom	Place of collection	Moisture (%)	Carbohydrate	Protein	Fat	Fibre	Reference
Armillaria mellea	Darjeeling	92.27	60.08	24.47	2.8	15.8	Rai *et al.,* 2007c
Astraeus hygrometricus	Bankura	ND	64.33	16.47	3.2	10.8	Biswas *et al.,* 2010c
Auricularia auricula	Darjeeling	94.7	53.5	19.8	2.7	15.9	Acharya *et al.,* 2002
Clitocybe sp	Darjeeling	90.8	46.9	24.6	3.67	9.2	Acharya *et al.,* 2004a
Collybia sp	Darjeeling	93.58	41.28	20.63	4.2	6.42	
Ganoderma applanatum	Darjeeling	73.9	30.1	15	1.5	45.2	Acharya *et al.,* 2002
Lentinus squarrosulus	Coastal region	91.25	ND	21.54	4.63	8.71	Giri *et al.,* 2013
Meripilus giganteus	Darjeeling	89	53.7	21.2	2.2	23.46	Acharya and Rai 2013
Oudemansiella mucida	Darjeeling	ND	46.9	24.6	3.67	9.2	Rai *et al.,* 2007b
Polyporus gramocephalus	Darjeeling	89.1	41.11	20.6	2.03	ND	Rai and Acharya 2004
Ramaria botrytis	Darjeeling	90.34	40.14	19.32	2.47	27.57	Rai *et al.,* 2006
Russula alatoreticula	Lateritic region	91.33	63.56	22.34	2.11	10.06	Khatua *et al.,* 2021b
Russula albonigra	Gangetic plain	92.5	ND	24.7	1.2	5.4	Giri *et al.,* 2013
Sparassis crispa	Darjeeling	ND	37.58	7.11	3.9	27.18	Acharya *et al.,* 2004b
Tricholoma giganteum	Lateritic region	90.4	ND	16.7	3.1	12.5	Giri *et al.,* 2013

ND: Not detected

deed, a person with weekend immune system becomes more susceptible to infections which are generally treated with antibiotics. Therefore, searching for new biomaterials that can potentiate the immune function has been of great interest in immune-pharmacological and onco-therapeutic research (Lee *et al.* 2013).

Our research identified many wild edible mushrooms with immune enhancing property *in vitro*. Pure polysaccharide isolated from *T. crassum* and *R. albonigra induced* NO production by murine macrophage and stimulated splenocyte and thymocyte proliferation (Patra *et al.,* 2012; Nandi *et al.,* 2012; Samanta *et al.,* 2013; Nandi *et al.,* 2013; Nandi *et al.,* 2014). Alongside, purified glucan from *E. lividoalbum* and *Lentinus fusipes* enhanced malondialdehyde (MDA), NO, oxidized glutathione (GSSG) and decreased reduced glutathione (GSH) level without causing cellular damage to human lymphocyte (Maity *et al.*, 2014a; Manna *et al.,* 2017). Alongside we have isolated crude polysaccharidic fractions from *R. alatoreticula, R. senecis* and *M. lobayensis* where preparations exhibited strong immune boosting property marked by augmentation of murine macrophage viability, phagocytosis and production of NO, ROS as well as filopodia/ lamellipodia. Thereafter, significant increase in TLR-2, TLR-4, NF-κB, COX2, TNFa, IκBa, IFγ and iNOS expression were also observed explaining mode of action through TLR/ NF-κB pathway. Consequently, water fractions among the polysaccharidic preparations confirmed better potential and that could be due to presence of different monomers in higher extent andorganization of the backbone in triple helical conformation (Khatua *et al.,* 2017a; Khatua and Acharya 2017; Khatua and Acharya, 2018b; Khatua and Acharya, 2019; Ghosh *et al.,* 2019; Khatua and Acharya, 2021b; Khatua *et al.,* 2021a). Similar trend of effect was also noted in case of *C. indica* where crude polysaccharide enhanced expression of pro-inflammatory cytokines and activated NF-κB signaling pathway by overexpressing MyD88, Iκ-Ba and NF-κB (Ghosh *et al.,* 2021).

Nitric oxide synthase activity

Nitric oxide is formed enzymatically from L-arginine

Table 3 : Antioxidant activity of studied wild and cultivated edible mushrooms of West Bengal as represented by EC_{50} values (ig/ml). ND: Not determined

Name of mushroom	Place of collection	Extract/ pure component	1	2	3	4	5	Reference
Agrocybe pediades	Murshidabad	Methanol	ND	ND	1030	ND	ND	Acharya *et al.*, 2017f
Amanita vaginata	Forest of Midnapur	Hydro-ethanol	10	1200	1450	1750	1550	Paloi and Acharya, 2013
		Ethanol			1480	730	910	Paloi and Acharya, 2014
Armillaria mellea	Darjeeling	Water	389	ND	106	ND	ND	Rai *et al.*, 2009
		Boiled water	220	ND	92	ND	ND	
		Ethanol	36	ND	107	ND	ND	
Astreus hygrometricus	Market of Bankura and West Midnapore	Water	ND	502	ND	ND	ND	Biswas *et al.*, 2010a
		Boiled water	ND	532	ND	ND	ND	
		Ethanol	ND	358	ND	ND	ND	
Auricularia auricula	Darjeeling	Water	403	ND	ND	ND	ND	Acharya *et al.*, 2004c
		Boiled water	510	ND	ND	ND	ND	
		Ethanol	373	ND	ND	ND	ND	
Calocybe indica		Methanol extract	ND	ND	957	ND	ND	Acharya *et al.*, 2016e
Entoloma lividoalbum	Darjeeling	β-D-glucan	480	150	ND	390	480	Maity *et al.*, 2014b
		β-glucan	400	75	ND	ND	470	Maity *et al.*, 2015
		Ethanol	ND	ND	ND	4400	480	Dasgupta *et al.*, 2015
		Methanol	ND	ND	978	ND	ND	Acharya *et al.*, 2017a
Ganoderma applanatum	Darjeeling	Water	604	ND	ND	ND	ND	Acharya *et al.*, 2005
		Boiled water	624	ND	ND	ND	ND	
		Ethanol	268	ND	ND	ND	ND	
Grifola frondosa	Darjeeling	Methanol	ND	ND	666	ND	ND	Acharya *et al.*, 2015a
Laetiporus sulphureus	Coastal area	Methanol	ND	1380	110	270	260	Acharya *et al.*, 2016d

Lentinus sajor-caju	Baruipur	Methanol	ND	ND	430	ND	ND	Acharya *et al.,* 2017b
		Heteroglycan	1310	ND	ND	2670	1750	Pattanayak *et al.,* 2018
Lepista sordida	Gangetic plains of Murshidabad	Decoction	ND	ND	210	410	3440	Acharya *et al.,* 2018
		Infusion	ND	ND	200	610	3010	
		Methanol	ND	ND	330	177	160	Acharya *et al.,* 2019a
Macrocybe crassa	Coastal area	Ethanol	ND	640	1660	530	ND	Khatua and Acharya 2014
		Methanol	ND	ND	2455	ND	ND	Acharya *et al.,* 2015b
Macrocybe gigantea	Market of Kolkata	Water	94	472	ND	ND	ND	Banerjee *et al.,* 2007
		Boiled water	81	602	ND	ND	ND	
		Ethanol	74	350	ND	ND	ND	
	Coastal area	Hot water extracted crude polysaccharide	693	82	1330	43	1630	Khatua and Acharya, 2016
		Cold alkali extracted crude polysaccharide	903	412	1870	73	2580	
		Hot alkali extracted crude polysaccharide	862	690	1950	88	2730	
Macrocybe lobayensis	Coastal area	Methanol	ND	ND	611	990	1786	Khatua *et al.,* 2017c
		Ethanol	ND	ND	1050	1000	ND	Khatua and Acharya, 2018a
		Hydro-ethanol	41	827	645	263	1783	Khatua *et al.,* 2019b
		Hot water extracted crude polysaccharide	444	ND	ND	ND	ND	Ghosh *et al.,* 2019
Macrolepiota dolichaula	Vidyasagar University garden	Fucogalactan	875	80	ND	ND	ND	Samanata *et al.,* 2015
Meripilus giganteus	Market of Darjeeling	Ethanol	71	ND	ND	ND	ND	Acharya and Rai, 2013

		Glucan	390	70	ND	290	ND	Maity *et al.,* 2017
		Methanol	ND	ND	400	ND	ND	Acharya *et al.,* 2017c
Oudemansiella canarii	Gangetic plains	Methanol	ND	ND	912	ND	ND	Acharya *et al.,* 2019b
Pleurotus djamor	Cultivation center	Methanol	ND	ND	653	ND	ND	Acharya *et al.,* 2017d
		Galactoglucan	1681	ND	3830	ND	4258	Maity *et al* ., 2021
Pleurotus eous	Cultivation center	Infusion	640	ND	97	ND	ND	Ghosh *et al.,* 2020
		Decoction	ND	ND	81	ND	ND	
Pleurotus flabellatus	Market of Darjeeling	Ethanol	ND	ND	1800	260	840	Dasgupta *et al.,* 2013
		Hydro-ethanol	ND	710	480	720	870	Dasgupta *et al.,* 2014c
Pleurotus florida	Cultivation center	Crude polysaccharide	140	320	ND	450	2000	Saha *et al.,* 2013
		Infusion	526	ND	108	ND	13	Ghosh *et al.,* 2020
		Decoction	ND	ND	71	ND	11	
Pleurotus ostreatus		Heteroglycan from mycelial culture	943	53	ND	1000	ND	Patra *et al.,* 2013
	Cultivation center	Crude polysaccharide	665	390	ND	370	ND	Mitra *et al.,* 2013
		Methanol		ND	1232	ND	ND	Acharya *et al.,* 2016a
		Infusion	554	ND	105	ND	14	Ghosh *et al.,* 2020
		Decoction	ND	ND	83	ND	13	
Pleurotus squarrosulus	Lateritic area	Cold water	364	1830	465	90	1330	Pal *et al.,* 2010
		Hot water	268	1473	340	75	1140	
		Methanol	706	8630	1500	1225	13000	
Polyporus grammocephalus	Darjeeling	Water	394	ND	125	ND	ND	Rai *et al.,* 2007a
		Boiled water	300	ND	92	ND	ND	
		Ethanol	62	ND	129	ND	ND	
Ramaria aurea	Market of Darjeeling	Ethanol	65	ND	ND	ND	ND	Rai and Acharya, 2012b

		Hydro-ethanol	ND	283	384	950	560	Khatua *et al.,* 2015b
Ramaria botrytis	Forest and market of Darjeeling	Water	205	ND	123	ND	ND	Rai *et al.,* 2008
		Boiled water	325	ND	92	ND	ND	
		Ethanol	47	ND	117	ND	ND	
Russula alatoreticula	Lateritic area	Hot water extracted Crude polysaccharide	1305	742	1328	190	1237	Khatua *et al.,* 2017a
		Hydro-ethanol	75	ND	2450	3615	ND	Khatua *et al.,* 2018c
		Cold alkali extracted crude polysaccharide	1848	ND	1976	283	1687	Khatua and Acharya, 2019
		Methanol extract	ND	1940	1083	263	2382	Khatua *et al.,* 2019a
		Hot alkali extracted crude polysaccharide	1435		1855	220	5000	Khatua *et al.,* 2021a
		Ethanol	ND	ND	785	1500	2500	Khatua *et al.,* 2021b
Russula albonigra	Lateritic area	β-glucan	265	130	ND	300	500	Nandi *et al.,* 2014
		Hydro-ethanol	ND	740	470	ND	1120	Dasgupta *et al.,* 2014b
		Ethanol extract	ND	740	1700	810	690	Dasgupta *et al.,* 2014a
Russula senecis	Lateritic area	Hydro-ethanol	5	ND	1340	158	2495	Khatua *et al.,* 2015
		Cold alkali extracted crude polysaccharide	892	872	1960	257	4068	Khatua and Acharya, 2017
		Hot water extracted crude polysaccharide	403	360	1387	80	3885	Khatua and Acharya, 2018b
		Ethanol extract	ND	272	739	122	437	Khatua and Acharya, 2021a
		Hot alkali extracted crude polysaccharide	844	ND	2909	225	1417	Khatua and Acharya, 2021b
Schizophyllum commune	Coastal area	Methanol	ND	ND	1070	ND	ND	Acharya *et al.,* 2016c
Termitomyces clypeatus	West Midnapore	Heteroglycan	ND	180	ND	ND	260	Pattanayak *et al.,* 2015

		Ethanol	ND	330	3220	210	1770	Mitra *et al.,* 2016
		Hydro-ethanol	8250	350	330	1008	ND	Mitra *et al.,* 2017
Termitomyces heimii	Midnapore	Ethanol	ND	ND	1250	ND	575	Mitra *et al.,* 2015
		Hydro-ethanol	21	190	490	ND	1310	Mitra *et al.,* 2016b
Termitomyces medius	West Midnapore	Ethanol	ND	1400	500	680	2050	Mitra *et al.,* 2014b
		Hydro-ethanol	19	425	600	540	1550	Mitra *et al.,* 2019
		Hot water extracted crude polysaccharide	960	410	ND	150	1950	Mitra *et al.,* 2021
Termitomyces microcarpus	Birbhum	Ethanol	ND	295	1980	140	1650	Mitra *et al.,* 2014a
		Hydro-ethanol	ND	350	600	1300	1700	Mitra *et al.,* 2016a
Volvariella volvacea	Gangetic plain	Water	302	ND	607	ND	ND	Rai and Acharya, 2012c
		Boiled water	215	ND	528	ND	ND	
		Ethanol	86	ND	256	ND	ND	
	Coastal area	Methanol	ND	ND	120	ND	ND	Acharya *et al.,* 2016b

1: Hydroxyl radical scavenging assay 2: Superoxide radical scavenging assay 3: DPPH radical scavenging assay 4: Chelating ability of ferrous ion 5: Reducing assay

in presence of nitric oxide synthase (NOS). Modulation of the molecule may help in treatment of a variety of diseases and the approach has become a target for new drug development. The high level of flavonoids, catechins, tannins and other polyphenolic compounds present in herbs is believed to contribute to their beneficial health effects. As a result, many botanical medicinal herbs and drugs derived from them have been shown to possess effects on NO signaling pathway (Achike and Kwan 2003).

We surveyed on NOS activity of wild edible mushrooms from West Bengal. Results revealed that numerous specimens namely *A. auricula* (Acharya *et al.,* 2004c), *G. applanatum* (Acharya *et al.*, 2005), *P. grammocephalus* (Rai *et al.*, 2007a), *M. gigantea* (Banerjee *et al.,* 2007), *R. botrytis* (Rai *et al.,* 2008), *A. mellea* (Rai *et al.,* 2009), *A. hygrometricus* (Biswas *et al.,* 2010a), *V. volvacea* (Rai and Acharya, 2012a), *R. aurea* (Rai and Acharya, 2012b), *M. giganteus* (Acharya and Rai, 2013), *P. ostreatus* (Mitra *et al.,* 2013), *P. florida* (Saha *et al.,* 2013) showed significant increase in NO production over control. Amongst the studied fractions, ethanolic preparation exhibited better potential than water fraction.

Hepato-protective effect

Hepatic disease might be caused by several biological factors (bacteria, virus, and parasites), autoimmune disease (immune hepatitis, primary biliary cirrhosis), action of different chemicals, and excessive consumption of alcohol. Despite enormous advances in modern medicine, there are no effective drugs that can offer complete protection to the organ. Thus, it is necessary to identify more effective and less toxic alternative pharmaceuticals for the treatment (Madrigal-Santillán *et al.,* 2014).

In this context, our research team has investigated the hepatoprotective activity of ethanolic extract of *R. albonigra* (Chatterjee *et al.,* 2012), *M. gigantea* (Acharya *et al.,* 2012a), *C. indica* (Chatterjee *et al.,* 2011) and *A. hygrometricus* (Biswas *et al.,* 2011b). The fractions were orally administered to the tasted animals where hepatotoxicity was induced by carbon tetrachloride (CCl_4). Serum glutamate oxaloacetate transaminase, serum glutamate pyruvate tranaminase, alkaline phosphatase and bilirubin content which was elevated due to CCl_4 intoxication was significantly reduced by all of the studied extracts. The hepatic antioxidant status such as catalase, superoxide dismutase, reduced glutathione levels were reduced in the CCl_4 alone treated animals with subsequent increase in lipid peroxidation. The hepatoprotective activity was further supported by histopathological studies of liver tissue.

Anti-diabetic activity

Today, another major public health problem at global scale is diabetes mellitus. This metabolic disorder of multiple etiologies is distinguished by a failure of glucose homeostasis with disturbances of carbohydrate, fat and protein metabolism as a result of defects in insulin secretion and/or insulin action. Cardiovascular diseases, nephropathy, neuropathy, and retinopathy are among the major risks. The consequence may lead to atherosclerosis resulting coronary heart disease, stroke, and other blood vessel diseases, kidney failure, nerve damage, and blindness with time

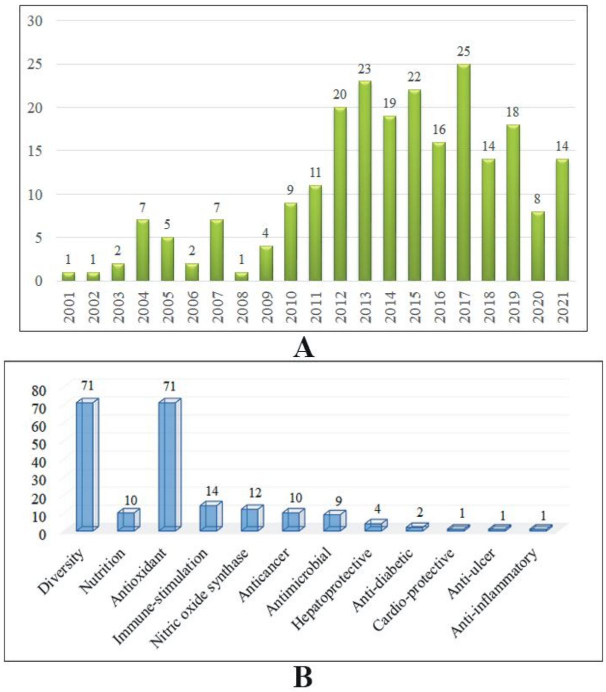

Fig. 1: Papers published by our team on diversity and determination of nutraceutical property of wild and cultivated mushrooms of West Bengal since past 20 years. A. Year wise publication B. Publication in different areas

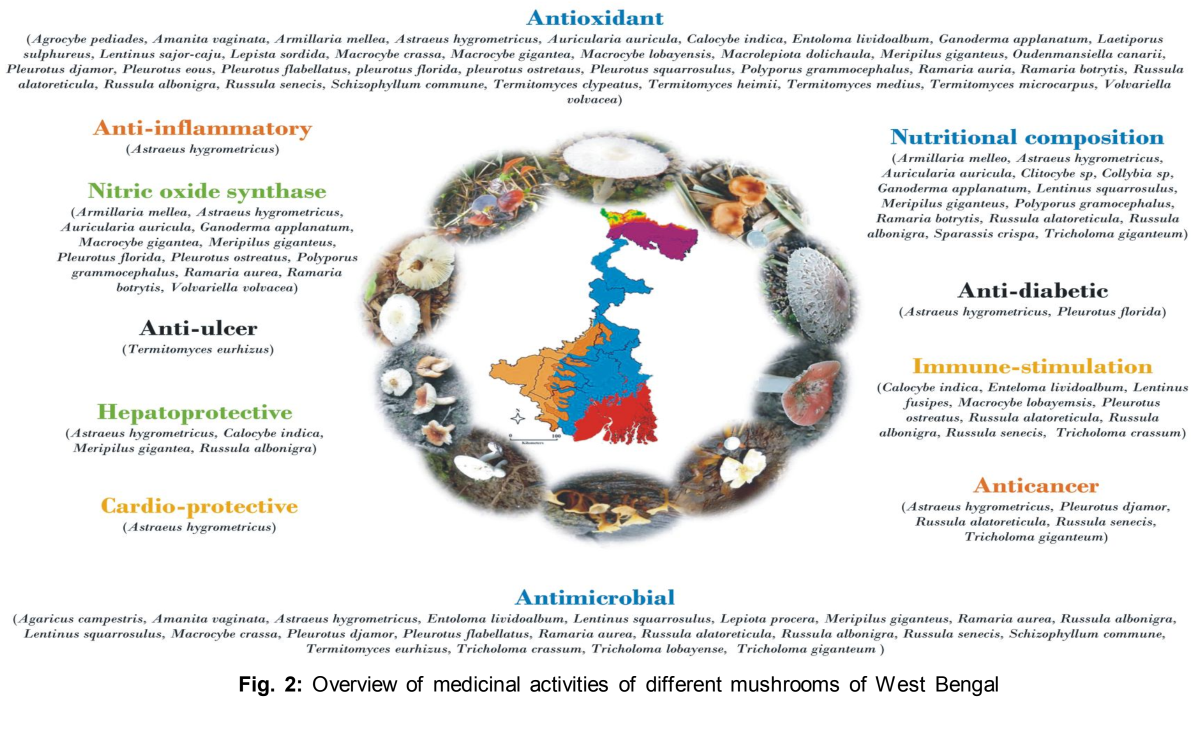

Fig. 2: Overview of medicinal activities of different mushrooms of West Bengal

(Tafesse *et al.,* 2017).

In this context, we have reported hypoglycemic effects of ethanolic extract of A. hygrometricus in alloxan-induced diabetic mice. Administration of the extract orally reduced blood glucose level in diabetic mice and showed better tolerance to glucose (Biswas and Acharya, 2013). Alongside effect of crude polysaccharide from *P. florida* has also been examined, however in combination with an established anti-diabetic drug, i.e, metformin. Results exhibited decline in blood glucose level in both acute and sub-acute studies in group of mice having combined treatment. The treatment also reduced ROS formation in liver protecting the organ from oxidative stress (Sultana *et al.,* 2014).

Cardio-protective effect

Cardio-vascular diseases (CVD)s are a variety of diseases including peripheral vascular diseases, coronary heart disease, heart failure, heart attack, stroke, cardiomyopathies, dyslipidemias, and hypertension, among others. The disease majorly originates from a vascular dysfunction due to atherosclerosis, thrombosis, and high blood pressure (BP). Common risk factors include smoking, unhealthy diet, diabetes mellitus, hyperlipidemia, elevated levels of low-density lipoprotein cholesterol (LDL), suppressed levels of high-density lipoprotein cholesterol (HDL), and hypertension (Shaito *et al., 2020).*

Our investigation showed that incubation of platelet rich plasma with ethanolic extract of A. hygrometricus resulted in inhibition of both secondary phase of adenosine diphosphate (ADP) induced platelet aggregation and prostaglandin synthesis with simultaneous stimulation of NO production. The result also suggested that fraction may have a role in preventing development and progression of hypertrophy. Thus, the extract might reduce incidence of cardiac hypertrophy, first myocardial infarction, recurrent infraction and vascular death among patients with cardiovascular disease (Biswas *et al.,* 2011a).

Anti-ulcer activity

Ulcer is a common gastrointestinal disorder and can be characterized by inflamed lesions of mucosa and tissue that protect gastrointestinal tract. Damage of mucus membrane which normally protects oesophagus, stomach and duodenum from gastric acid and pepsin causes ulcer. The pathogenesis of gastric ulcers remains widespread, it is multifactorial disease where diverse factors such as infection by Helicobacter pylori, alcohol consumption, inappropriate food habits, stressful lifestyle, use of steroidal and nonsteroidal anti-inflammatory drugs (NSAIDs) and drugs which stimulate gastric acid and pepsin secretion, smoking and so forth. The available drugs are expensive and are likely to produce more side effects (Pahadiya and Sisodia, 2018). In contrast herbal drugs and formulations which possess potent antioxidant property are effective in healing experimentally induced gastric ulcer.

Our study aimed to determine healing activity of water soluble polysaccharide-rich fraction of *T. eurhizus* against indomethacin induced gastric ulceration in mice model. Histological analysis revealed that the extract effectively healed gastric ulceration and the effect could be attributed to reduction of myeloperoxidase activity and protection of mucosal mucin content. Enhanced synthesis of prostaglandin E2 by modulation of cyclooxygenases (COX)-1 and COX-2 expression and a prominent shift of cytokines expression from pro (TNF-a, IL-1ß) to anti-inflammatory (IL-10) side were also held responsible for ulcer healing (Chatterjee *et al.,* 2013a).

Anti-inflammatory activity

Inflammation is a defense response of our body to hazardous stimuli such as allergens and/or injury to tissues; while, uncontrolled inflammatory response is the main cause of various disorders including cancer, cardiovascular dysfunctions, metabolic syndrome, allergies, and autoimmune diseases. There are various medicines for controlling and suppressing inflammatory crisis which are associated with adverse effects. Hence there is a need for the development of potent analgesic and anti-inflammatory drugs with fewer side effects (Ghasemian *et al.,* 2016).

In this context, we have investigated on anti-inflammatory activity of ethanolic extract from *A. hygrometricus* in carrageenan and dextran induced acute and formalin induced chronic inflammatory model in mice. The fraction significantly reduced the carrageenan and dextran induced paw oedema. The extract was also effective in ameliorating formalin induced chronic inflammation. The outcome was highly comparable to a standard drug, diclofenac (Biswas *et al.,* 2010b).

CONCLUSION AND FUTURE PROSPECTS

All in all, West Bengal macrofungal flora encompasses several unique featured taxa growing naturally all-over the state. Many of these wild specimens possess high nutritional value supporting their ethnic consumption as gourmet cuisine. In addition, multi-therapeutic effects have also been revealed where the organic fractions showed potent antioxidant, antimicrobial, anti-cancer effects; whilst polysaccharidic compound displayed a critical role in enhancing immune strength. Hence there is a huge challenge for better utilization of this wonderful gift of nature and bring it forward from the field to industry level motivating us for further investigations. The endeavor is thus in continuation with an aim of exploitation of wild mushrooms of West Bengal as sources of effective, and safe world-class new medicines dietary supplements to serve humankind.

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