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Review Article

Mushroom: a potent source of natural antiviral drugs

Jay Kant Raut *
Bioresource Laboratory, Nepal Academy of Science & Technology, Khumaltar, Lalitpur, PO Box 3323, Nepal
ORCID ID: 0000-0002-9484-1999, Tel: 9841300540

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Abstract: Emerging viral infections such as the zika virus, dengue virus, ebola virus, corona virus are afflicting millions of human populations worldwide. Therefore, the development of new treatments against emerging infectious diseases has become an urgent task. The availability of commercially viable, safe, and effective antiviral drugs still remains a big challenge. Mushrooms are considered as an untapped reservoir of several novel compounds of great value in industry and medicine. Although exploration, and exploitation of the therapeutic importance of fungal metabolites has started early with the discovery of penicillin, mushrooms's pharmacological potential has much less been investigated. This article briefly reviews the antiviral potentials of mushrooms to combat deadly disease outbreaks caused by emerging and re-emerging viruses. Altogether 69 mushroom species with potent antiviral agents and mode of action against prominent viruses such as human immunodeficiency virus, influenza, herpes simplex virus, hepatitis B and C viruses, corona viruses etc. are listed in this study. Further studies are encouraged to discover more novel potent antiviral agents or evaluate already known compounds from those mushrooms with clinical trials.

Keywords: *bioactivity; COVID-19; fungi; metabolites; pandemic*

सारांशः प्राचीन फिरन्ते सिकारी युगदेखि अहिलेको आधुनिक युगसम्म आइपुग्दा मानवजातिले कैयौं सरुवा महामारीको सामना गर्दै अगाडी बढेको छ । यी मध्ये भाइरल संक्रमण सबभन्दा खतरनाक र प्रमुख विश्वव्यापी स्वास्थ्य समस्याहरू मध्येको एक हो । विगत सय बर्षमा मात्रै भाइरल संक्रमणले बारम्बार ठूलो मानवीय क्षति गर्नुको साथै विश्वव्यापीरुपमा गम्भीर आर्थिक संकट समेत सृजना गरेको छ । विश्व हाल कोभिड-१९को गम्भीर संकटबाट गुज्रिरहेको छ । फ्लू भाइरस, जिका भाइरस, डेंगू भाइरस, इबोला भाइरस, कोरोना भाइरस जस्ता उदीयमान भाइरल संक्रमणले विश्वभरि करोडौं मानव जनसंख्यालाई पिरोलेको छ । त्यसकारण उदाउँदो भाइरसजन्य संक्रामक रोगहरूको बिरूद्ध नयाँ उपचारको खोजी तथा विकास गर्नु अत्यन्त जरुरी छ । हालसम्म व्यावसायिक रूपमा धान्न सकिने, सुरक्षित र प्रभावकारी भाइरसप्रतिरोधी औषधीहरूको विकास हुन सकेको छैन । औषधी लगायत विभिन्न उद्योगहरूको लागि उपयोगि कैयौं नविन यौगिकहरूको लागि च्याउ अमूल्य भण्डारको रूपमा रहेको कुरा विभिन्न अध्ययनहरूबाट देखिएको छ । फन्गल मेटाबोलिट्सको चिकित्सीय महत्वको खोज तथा अनुसन्धान महत्व्पूर्ण औषधी पेनिसिलिनको आविष्कार भएसँगै भएतापनि च्याउहरूको औषधीय सम्भावनाको खोज तथा अनुसन्धान अत्यन्तै न्यून रहेको पाइन्छ । यस लेखमा भाइरसजन्य संक्रामक घातक रोगहरूसँग लड्न च्याउहरूको भाइरसप्रतिरोधी क्षमताहरूको संक्षिप्तरुपमा समीक्षा गरिएको छ । यसमा ६९ च्याउ प्रजातिहरूमा पाइएका शक्तिशाली भाइरसप्रतिरोधी पदार्थहरु र प्रमुख भाइरसहरू जस्तै मानव इम्युनोडेफिशियन्सी भाइरस, इन्फ्लूएन्जा, हर्पेस सिम्प्लेक्स भाइरस, हेपेटाइटिस बी र सी भाइरस, कोरोनाभाइरस आदि विरूद्ध कार्य गर्ने तरीका सूचीबद्ध गरिएको छ । अध्ययनले च्याउमा थप नविन शक्तिशाली भाइरसप्रतिरोधी पदार्थहरु पत्ता लगाउन र च्याउहरूबाट पहिल्यै ज्ञात यौगिकहरूको थप मुल्याङ्कन एवं क्लिनिकल परीक्षण गर्न प्रोत्साहन गर्नेछ भन्ने अपेक्षा गरिएको छ ।

* Corresponding author, E-mail: raut_jk2000@yahoo.com; Tel.: +977-9841300540

1. Introduction

Viral diseases are brutal killers and one of the leading global health threats (Pour et al., 2019). In the past 100 years, viral infections have repeatedly caused millions of human casualties and economic chaos worldwide. The Spanish flu (1918-1919), an influenza pandemic, caused approximately 50 million deaths (Centers for Disease Control and Prevention [CDC], 2014), and HIV/AIDS took the lives of more than 35 million (CDC, 2020). Although more recently emerging viral outbreaks such as severe acute respiratory syndrome (SARS) in 2003, H1N1 in 2009, Middle East respiratory syndrome (MERS) in 2012, Ebola in 2014, have had lower death tolls, however, they had a huge social and economic impact (Global Health Risk Framework for the Future [GHRF], 2016). Currently, the world is fighting with a novel Corona virus disease (COVID-19) pandemic. According to the World Health Organization (WHO), as of this writing on May 9, 2020, 3 767 744 cases have been confirmed with 259 593 death tolls among 215

Countries, areas, or territories around the globe (WHO, 2020). No vaccines and drugs are available for prevention, prophylaxis, and treatment of corona virus infections in humans (Eurosurveillance Editorial Team, 2020). Therefore, to find new preventive and therapeutic agents against emerging infectious diseases has become an urgent task. Virus-specific vaccines and antiviral drugs are considered as the most powerful tools to combat infectious outbreak diseases. A new era of antiviral drug development has begun since the first antiviral drug, idoxuridine, was approved in June 1963 (De Clercq, 1997). A freely accessible database (https://drugvirus.info/) contains 120 approved, investigational and experimental safe-in-man broad-spectrum antiviral agents (BSAAs) which inhibit 86 human viruses, belonging to 25 viral families (Andersen et al., 2020). Almost all currently approved antiviral drugs are synthetic, produced by chemical synthesis. Recently great attention has paid to find novel, effective, and safe alternatives against viral diseases due to the rapid emergence of resistance, high costs, the related side effects, and cell toxicity of synthetic antiviral drugs (Farrar et al., 2007). There are several natural compounds that have already been identified as antiviral agents (Martins et al., 2016). About fifty percent of today's pharmaceutical drugs are derived from natural origin (Clark, 1996). In this regard, the discovery and production of antiviral metabolites from mushroom, a higher fungus, have emerged as part of an exciting field in viral therapeutic and antiviral drug development. This mini-review provides an insight into the mushrooms and their metabolites, explaining their potential role as major alternatives in the treatment of various viral infections.

2. Antiviral Research and Mushroom Taxonomy

Mushrooms produce a plethora of biologically active secondary metabolites, including a wide variety of clinically important drugs. Cochran was the first to report the antiviral substances in mushrooms (Goulet et al., 1960). The active research on antiviral drug development started only after the discovery of the first viral enzyme DNA-dependent RNA polymerase of poxvirus in 1967 (Kates, 1967). Since then, mushrooms became a hunting ground for novel drug leads. Secondary metabolites from fungi represent a substantial fraction of our current pharmaceuticals, including the most popular antibiotic penicillin, immunomodulatory agents as well as those used as cholesterol-lowering (Newman and Cragg, 2016). Accurate taxonomy is paramount for the exploitation of the numerous advantages an organism offers, especially for pharmaceutical products (Raja et al., 2017). There is a serious issue of species identification in the mushroom antiviral research. In many studies, detailed information about the specimens is lacking (Linnakoski et al., 2018). Accurate species identification is a critical step to ensure the reproducibility of the work and can unlock important information regarding a species and its possible biochemical properties. Very few studies have included morphological and molecular methods both for species identification (Raja et al., 2017). The modern molecular technique reduces the challenges of inconspicuous nature, inconsistent morphology, and indiscrimination among fungal species often associated with the traditional method of nomenclature (Nilsson, 2011). A survey based on the fungal natural product articles published in the Journal of Natural Products during 2000-2015 reveals that∼31% provided fungal identification based solely on morphology; ∼28% of them did not report any form of identification for the fungus from which secondary metabolites were isolated; 27% of the studies used molecular data only (mostly from the internal transcribed spacer (ITS) region) for fungal identification; and ∼14% used a combination of morphology and molecular data (both rRNA and protein-coding genes) to identify fungi (Raja et al., 2017). This suggests that the proper taxonomic identification of fungi in natural product research need to be addressed more seriously.

Ganoderma lucidum is one of the most common mushrooms used in mushroom antiviral research. Most of the studies often cited *G. lucidum* as the species of the material. However, the exact delimitation of the species concept for *G. lucidum*, with a European type locality, has been difficult due to the lack of a holotype specimen (Steyaert, 1972). Based on molecular studies the industrially cultivated “Linghzi” and “Reishi” do not represent the *G. lucidum* s. str, but in fact, other species (Wang et al., 2009; Cao et al., 2012). Therefore, careful consideration is required when identifying such samples. In the advanced pharmacological exploitation of mushrooms, adoption of the recently suggested set of standard procedures and consultation of taxonomists for accurate species identification is paramount to avoid all kinds of taxonomical ambiguity.

3. Antiviral molecules of mushroom origin

After the discovery of the first wonder drug, Penicillin from filamentous fungi, much more attention has been carried out in therapeutic usage of fungus, especially from medicinal mushrooms. Medicinal mushrooms contain a wide range of various compounds, such as polysaccharides, organic acids, lipids, steroids, tetracyclic triterpenes, and many others displaying antitumor, immunestimulating, antibacterial, and antiviral effects which are of interest for medical applications. A large number of medicinal functions (>100) have been reported from mushrooms. More than 600 clinical trials with mushrooms on various health disorders have been performed, and approximately 15,000 patents associated with different aspects of mushrooms were issued (Wasser, 2017). From 2005, around 250–350 patents were registered each year for *Ganoderma lucidum* alone. Taiwanese scientists received more than 100 patents on one species from the genus *Antrodia* (Wasser, 2017). From this, it may be concluded that mushrooms are the most potent, natural immune force ever discovered, and hence it can be considered as a priceless asset for human welfare.

A wide range of antiviral agents has been reported from a number of mushroom species (Table 1). Antiviral effects of mushroom have been reported in whole extracts and isolated molecules that can be from both fruiting bodies and mycelia. Antiviral agents in mushrooms can be divided into two major groups of molecules; the high-molecular weight compounds such as polysaccharides, proteins and lignin-derivatives from the fruiting bodies exhibiting their effect indirectly through immunostimulating activity, and the low-molecular weight compounds small organic molecules excreted by mushrooms in a liquid culturing (fermentation) setups that directly inhibit viral enzymes, synthesis of viral nucleic acids or adsorption and uptake of viruses into cells (Brandt and Piraino, 2000). The concentration and efficacy of bioactive compounds are varied and depend on the type of mushroom, substrate, fruiting conditions, stage of development, age of mushroom, and storage conditions (Guillamón et al., 2010).

Table 1. Mushroom species with antiviral agents against various viruses and mode of action

Mushroom	Extract/Compound	Virus	Target/activity	Reference
Agaricus blazei	Extract	HBV	Supplement	Hsu et al. (2008)
		HCV	NA	Johnson et al. (2009)
Agaricus brasiliensis	Extract	Polio	NA	Faccin et al. (2007)
	Polysaccharide	HSV-1	Attachment/entry/ cell-to-cell spread	Cardozo et al. (2013)
	Polysaccharides	HSV-1, HSV-2	NA	Cardozo et al. (2014)
Agrocybe aegerita	Lectin	Influenza virus	Adjuvant	Ma et al. (2017)
Antrodia camphorata	Polysaccharides	HBV	NA	Lee et al. (2002)
Armillaria mellea	Extract	VSV	NA	Kandefer-Szersze et al. (1980)
Auricularia auricula	Polysaccharides	NDV	NA	Nguyen et al. (2012)
Auricularia polytricha	Hexane extract fraction	HIV-1, CoVs	Protease inhibitors	Sillapachaiyaporn et al. (2019)
Auriporia aurea	NA	HSV	NA	Hijikata et al. (2007)
	Extract	H1N1	NA	Krupodorova et al. (2014)
Boletus edulis	Extract, Polysachharide fraction	HSV-1	NA	Santoyo et al. (2012)
	Extract	Vaccinia virus	NA	Kandefer-Szersze et al. (1980)
Cerrena unicolor	LAC	HHV-1, EMCV	NA	Mizerska-Dudka et al. (2015)
Chondrostereum purpureum	Extract	HIV-1	RT	Mlinarič et al. (2005)
Collybia maculata	Purine derivatives	VSV	NA	Leonhardt et al. (1987)
Coprinus comatus	LAC	HIV-1	RT	Zhao et al. (2014)
Cordyceps militaris	Adenosine	HIV-1, CoVs	Protease inhibitor	Jiang et al. (2011)
	Iso-sinensetin	HIV-1, CoVs	Protease inhibitor	Jiang et al. (2011)
	Hemagglutinin	HIV-1	RT	Wong et al. (2009)
	Polysaccharide	influenza A virus	NA	Ohta et al. (2007)
Cryptoporus volvatus	Extract	H1N1, H3N2	NA	Gao et al. (2014)
Daedaleopsis confragosa	Extract	H1N1, H3N2	NA	Teplyakova et al. (2012)
Datronia mollis	Extract	H5N1, H3N2	NA	Teplyakova et al. (2012)
Elfvingia applanata	Extract	VSV	Adsorption	Eo et al. (2001)

Flammulina velutipes	FIP-Fve	HPV-16	Adjuvant	Ding et al. (2009)
	Extract	H1N1	NA	Krupodorova et al. (2014)
Fomes fomentarius	NA	HSV	NA	Hijikata et al. (2007)
	Extract	H1N1	NA	Krupodorova et al. (2014)
Fomitella supina	Extract	HIV-1	Virion inactivation, inhibition of syncytium formation	Walder et al. (1995)
Fuscoporia oblique	Water-soluble lignin	HIV-1	Protease inhibitor	Ichimura et al. (1998)
Ganoderma colossus	Ganomycin B	HIV-1, CoVs	Protease inhibitor	El Dine et al. (2008)
	Ganomycin I	HIV-1, CoVs	”	El Dine et al. (2008)
	Colossolactone A	HIV-1, CoVs	”	El Dine et al. (2008)
	Colossolactone E	HIV-1, CoVs	”	El Dine et al. (2008)
	Colossolactone G	HIV-1, CoVs	”	El Dine et al. (2008)
	Colossolactone V	HIV-1, CoVs	”	El Dine et al. (2008)
	Colossolactone VII	HIV-1, CoVs	”	El Dine et al. (2008)
	Colossolactone VIII	HIV-1, CoVs	”	El Dine et al. (2008)
	Lanostane triterpenes	HIV-1	”	El Dine et al. (2008)
Ganoderma lucidum	Extract	HBV	NA	Li and Zhang (2005)
	Ganoderic acid	HBV	NA	Li and Wang (2006)
	Ganolucidic acid A	HIV-1, CoVs	Protease inhibitor	El-Mekkawy et al. (1998)
	Ganoderic acid B	HIV-1, CoVs	”	Martínez et al. (2019)
	Ganoderic acid C1	HIV-1, CoVs	”	Martínez et al. (2019)
	Ganoderic acid β	HIV-1, CoVs	”	Martínez et al. (2019)
	Ganodermanondiol	HIV-1, CoVs	”	Martínez et al. (2019)
	Ganodermanontriol	HIV-1, CoVs	”	Martínez et al. (2019)
	Lucidumol B	HIV-1, CoVs	”	Martínez et al. (2019)
	GLPG	HSV-1, HSV-2	”	Liu et al. (2004)
	APBP	HSV-1, HSV-2	Entry/attachment	Eo et al. (2000)
	Extract	H1N1	NA	Krupodorova et al. (2014)
	LAC	HIV-1	NA	Wang and Ng (2006)
	Several triterpenoids	HIV	RT	Lindequist et al. (2005)
Ganoderma pfeifferi	Several compounds	HSV-1	NA	Lindequist et al. (2015)
Ganoderma sinnense	Ganoderic acid GS-1	HIV-1	Protease inhibitor	Sato et al. (2009)
	Ganoderic acid GS-2	HIV-1	”	Sato et al. (2009)
	Ganoderic acid DM	HIV-1	”	Sato et al. (2009)
	Ganoderic acid β	HIV-1	”	Sato et al. (2009)
	Ganoderiol A	HIV-1	”	Sato et al. (2009)
	Ganoderiol F	HIV-1	”	Sato et al. (2009)
	Ganodermadiol	HIV-1	”	Sato et al. (2009)
	Ganodermanontriol	HIV-1	”	Sato et al. (2009)
	Lucidumol A	HIV-1	”	Sato et al. (2009)
	20-hydroxylucidenic acid N	HIV-1	”	Sato et al. (2009)
	20(21)-dehydrolucidenic acid N	HIV-1	”	Sato et al. (2009)
Grifola frondosa	D-fraction	HBV	Combination	Gu et al. (2007)
	Mycelia extract	Enterovirus 71	Replication, RNA synthesis	Zhao et al. (2016)
	GFAHP	HSV-1	NA	Gu et al. (2007)
Hericium erinaceus	LAC	HIV-1	RT	Wang and Ng (2004a)
	Lectin	HIV-1	RT	Li et al. (2010)
Hohenbuehelia serotina	Ribonuclease	HIV-1	RT	Zhang et al. (2014)
Hypsizygus marmoreus	Sterols	EBV	NA	Akihisa et al. (2005)
	Marmorin	HIV-1	RT	Wong et al. (2008)
Inocybe umbrinella	Lectin	HIV-1	RT	Zhao et al. (2009)
Inonotus hispidus	Phenolic extracts	Influenza A, B	NA	Lindequist et al. (2005)

Inonotus obliquus	Polysaccharides	Feline H3N2, H5N6	Viral Binding/absorption	Tian et al. (2016)
	NA	HSV	NA	Polkovnikova et al. (2014)
	Extract	HSV	Entry	Pan et al. (2013)
	NA	HIV-1	NA	Shibnev et al. (2015)
Ischnoderma benzoinum	Extract	H5N1, H3N2	NA	Teplyakova et al. (2012)
Kuehneromyces mutabilis	Extract	Influenza viruses A, B	NA	Mentel et al. (1994)
Lactarius torminosus	Extract	HSV-1, HSV-2, PP, VSV	NA	Amoros et al. (2008)
Laetiporus sulphureus	Extract	HIV-1	RT	Mlinarič et al. (2005)
Laricifomes officinalis	Extract	H5N1, H3N2	NA	Teplyakova et al. (2012)
Lepista nuda	Metalloprotease	HIV-1	RT	Wu et al. (2011)
Lentinus edodes	Mycelia solid culture extract	HCV	Entry	Matsuhisa et al. (2015)
	JLS-S001	HSV	Assembly/budding	Sarkar et al. (1993)
	Extract	H1N1	NA	Krupodorova et al. (2014)
	Polycarboxylated water-solubilized lignin	HIV	Antigen expression	Suzuki et al. (1990)
	LAC	HIV-1	RT	Sun et al. (2011)
	JLS-18	Sendai virus	NA	Yamamoto et al. (1997)
Lenzites betulina	Extract	H5N1, H3N2	NA	Teplyakova et al. (2012)
Lignosus rhinocerus	Heliantriol F	HIV-1, CoVs	Protease inhibitor	Sillapachaiyaporn and Chuchawankul (2019)
Lyophyllum shimezi	Extract	H1N1	NA	Krupodorova et al. (2014)
Macrocystidia cucumis	NA	HSV-1	NA	Saboulard et al. (1998)
Omphalotus illudens	Illudin S	HSV-1	NA	Lehmann et al. (2003)
Phellinus baumii	Hispidin	H1N1, H5N1, H3N2	NA	Hwang et al. (2015)
	Hypholomine B	H1N1, H5N1, H3N2	NA	Hwang et al. (2015)
	Inoscavin A	H1N1, H5N1, H3N2	NA	Hwang et al. (2015)
	Davallialactone	H1N1, H5N1, H3N2	NA	Hwang et al. (2015)
	Phelligridin D	H1N1, H5N1, H3N2	NA	Hwang et al. (2015)
Phellinus igniarius	Sesquiterpenoid	Influenza virus	NA	Song et al. (2014)
	Extract	Influenza virus	NA	Lee et al. (2013)
Phellinus linteus	Extract	Influenza	Adjuvant (cross protection)	Ichinohe et al. (2010)
Phellinus pini	Extract	CVB3	plaque formation inhibition	Lee et al. (2009)
Phellinus rhabarbarinus	Extract	HIV-1	Virion inactivation, inhibition of syncytium formation	Walder et al. (1995)
Pholiota adipose	Lectin	HIV-1	RT	Zhang et al. (2009)
Pleurotus abalonus	LB-1b	HIV-1	RT	Li et al. (2012)
Pleurotus citrinopileatus	Lectins	HIV-1	RT	Li et al. (2008)
Pleurotus eryngii	Extract	H1N1	NA	Krupodorova et al. (2014)
	LAC	HIV-1	RT	Wang and Ng (2006)
Pleurotus ostreatus	LAC	HCV	NA	EL-Fakharany et al. (2010)
	Lectin	HBV	Adjuvant	Gao et al. (2013)
	Extract	H1N1	NA	Krupodorova et al. (2014)
	NA	HSV	NA	Hijikata et al. (2007)
	Ubiquitin-like protein	HIV-1	Protease	Wang and Ng (2000)

Pleurotus tuber-regium	Polysaccharides	HSV-1, HSV-2, RSV, Influenza A virus	Binding to the viral particles	Zhang et al. (2004)
Poria cocos	PCP-II	HBV	Adjuvant	Wu et al. (2016)
Poria monticola	Extract	HIV-1	RT	Mlinarič et al. (2005)
Poria vaillanti	Extract	HIV-1	RT	Mlinarič et al. (2005)
Rozites caperata	RC28 RC-183 RC28	HSV HSV-1, HSV-2 HSV-1	NA NA NA	Gong et al. (2009) Piraino and Brandt 1999) Yan et al. (2015)
Russula delica	Lectin	HIV-1	RT	Zhao et al. (2010)
Russula paludosa	4.5 kDa protein SU2	HIV-1, CoVs HIV-1	Protease inhibitor RT	Wang et al. (2007) Wang et al. (2007)
Schizophyllum commune	Extract Schizolysin	H1N1 HIV-1	NA RT	Krupodorova et al. (2014) Han et al. (2010)
Scleroderma citrinum	Triterpenoid	HSV	NA	Kanokmedhakul et al. (2003)
Trametes cubensis	Extract	HIV-1	Virion inactivation, inhibition of syncytium formation	Walder et al. (1995)
Trametes gibbosa	Extract	H5N1, H3N2		Teplyakova et al. (2012)
Trametes versicolor	Extract Extract NA	H5N1, H3N2 H1N1 HSV	NA NA NA	Teplyakova et al. (2012) Krupodorova et al. (2014) Hijikata et al. (2007)
Trichaptum perrottetti	Extract	HIV-1	Virion inactivation, inhibition of syncytium formation	Walder et al. (1995)
Tricholoma giganteum	LAC	HIV-1	RT	Wang and Ng (2004)

AIDS acquired immunodeficiency syndrome, APBP acidic protein-bound polysaccharide, c-EPL crude extract of endopolysaccharides, CMV cytomegalovirus, CoVs Corona viruses, CVB3 Coxsackievirus B3, EBV Epstein-Barr virus, EMCV encephalomyocarditis virus, FIP-Fve immunomodulatory protein, GLPG Ganoderma lucidum proteoglycan, GLTA Ganoderma lucidum triterpenoids Lanosta-7,9(11),24-trien-3-one,15;26-dihydroxy, HBV hepatitis B virus, HCV hepatitis C virus, HHV human herpesvirus, HIV human immunodeficiency virus, HPV human papillomavirus, HSV herpes simplex virus, HTLV human T-cell lymphotropic virus, JLS Water-soluble lignin-rich fraction, KS-2 extract from culture mycelia of Lentinus edodes, LB-1b a polysaccharide–protein complex, LAC laccase, NA not available, NDV Newcastle disease virus, PCP-II a new polysaccharide, PV poliovirus, RC a protein, RSV respiratory syncytial virus, RT Reverse transcriptase, SU2 a peptide, VSV vesicular stomatitis virus, VZV varicella zoster virus

4. Challenges and Future Avenues

Humankind has repeatedly been facing the great threat of deadly disease outbreaks caused by emerging and re-emerging viruses such as the Nipah virus, Hendra virus, Hantavirus, Ebola virus, SARS, MERS, Zika, Influenza virus, Corona viruses. To combat these viruses efficient and safe antiviral drugs need to be developed. Mushrooms are a great source for novel pharmaceuticals invention. Modern drug discovery which has its roots in traditional medicine provides avenues to newer mycomolecules-based therapies (Paterson and Anderson, 2005). There are a large number of structurally diverse metabolites from numerous fungal species. Among them, more than 15 fungal metabolites have already approved by the Food and Drug Administration (FDA) and some of these are still dominating the drug market. Currently, many fungal metabolites are at different stages of the drug development process (Aly et al., 2011).

On the other hand, only a small fraction of fungal species have been identified so far (Hawksworth and Lücking, 2017), and much less have been scientifically investigated for bioactive metabolites. As biological diversity implies chemical diversity, there is huge scope for finding many other potential drug lead through the exploration of new fungal species, their metabolites, and bioactivity. Ease of cultivation or culture of fungal species at a reasonable time and cost will be another big beneficial aspect of fungal metabolites. With an efficient and enhanced capability through high throughput screening facility, which is currently lacking in most fungal diversity rich countries, the antiviral fungal metabolite exploration process can be speed up.

5. Conclusions

Mushrooms metabolites with great diversity and preapproved biocompatibility can be a potential source for new antiviral drug lead. Considering, the discovery of a very small fraction of fungal species and only few percent of these fungal metabolites are investigated for various viral diseases indicates an enormous potential for finding new fungal metabolites as drug leads with a novel mechanism of action. This needs an energetic endeavor toward exploration, identification, and exploitation of unknown fungal species and developing better culture methods for drug discovery. The majority of the investigations were limited to basic screening and no mechanism of action was established for active metabolites so far. To develop commercial antiviral drugs from mushrooms, in vivo and clinical studies are other aspects that should be exploited. In addition, the establishment of more and more sophisticated antiviral screening facilities will be very helpful and a big boost to future antiviral drug discovery research.

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