STUDY OF SECONDARY METABOLITES PRODUCED BY WHITE ROT FUNGI FOR KNOWING THEIR ANTIMICROBIAL PROPERTIES

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Abstract : White rot fungi is a group of basidiomycetes mainly responsible for the degradation of wood components such as lignin, cellulose and hemicellulose responsible for causing white rot on wood. They plays an important role in carbon cycle and nitrogen cycle by balancing the carbon and nitrogenous components within the environment and create an eco-physiological group of diversity with others species. They produces a large no of primary and secondary metabolites during growth and developments such as several enzymes, amino acids, proteins, carbohydrates, alcohols, lipids and fatty acids. They are saprophytic and competes with other organisms during colonization on tree or other organic substances and inhibit the growth of other organisms by producing several components. White rot fungi are of the abundant source of natural antimicrobial components as they produce various bioactive secondary metabolites. Studies has been shown that the metabolites they produces having different biological functions such as anti-microbials, anti-parasites, insecticides, anti-tumor, anti-inflammation, anti-cancerous and anti-aging etc. beside these properties they are consumed as functional foods because of nutraceutical properties such as they contains vitamins, proteins, dietary fiber, low fats, lipids, minerals and watery substances that are very much essential and beneficial to human health and act against diseases.

Keywords- White Rot Fungi, Antimicrobial, Metabolites, Enzymes, Biosynthetic pathways, Nutraceuticals.

I. INTRODUCTION

Phylum Basidiomycota belongs to a large group that contains one third, around 32% of entire fungal diversity (Riley *et al.*, 2014), comprising at least 30,000 different species within them showing varieties of relationships like, mutualism, symbiosis, parasitism, etc. (Webster and Weber 2007). Basidiomycota are basically known as basidiomycetes (Hibbett *et al.*, 2007). They are ubiquitous in nature and can grow everywhere life is possible on Earth (Goyal *et al.*, 2018) and are evolved in terrestrial ecosystem as well as in marine habitat (Webster and Weber 2007).They are saprophytic fungus grows on dead organic materials like wood, waste organic materials, dead animals and other biological sources (Naresh Magan, 2008).

White rot fungi a group of basidiomycetes produces a great variety of different cellular enzymes such as hydrolytic and extracellular enzymes like cellulases, laccases, peroxidases and others (Alves *et al.*, 2010 ,Wang *et al.*, 2018).An important feature of basidiomycetes is the ability of degrading various components of wood and other organic materials including carbohydrates, polysaccharides and other biopolymeric substances and release carbon di-oxide , nitrogenous compound and water into the environment that plays a vital role in earth's ecosystem as well as in carbon cycle(Glazunova *et al.*, 2018, Baldrian *et al.*,2008).

As a result of degradation of various components of wood became pale and fibers like materials and cause rot on wood (Muthuthanthriege *et al.*, 2016).Based on the action of wood decaying a group of Basidiomycetes have been classified into brown rot and white rot and sometimes cause soft rot based on their ability of degradation. Brown rot and soft rot fungi responsible for degradation of cellulosic and hemi-cellulosic materials (Wang *et al.*, 2018, T Yilkal 2015). The white rot fungi is mainly responsible for the degradation of lignin by producing extracellular enzyme called lignin peroxidase (Sevindik *et al.*, 2018). They showed a wide range of biological properties like they can be poisonous, edible with degrading, nutritional and therapeutic properties (Ukwuru *et al.*, 2018, Remya *et a*l., 2019, and Sharma *et al*., 2017).

A large group of basidiomycetes are known for producing fruiting bodies called as mushrooms (Swann and Hibbett 2007). Mushroom is being considered as functional food from the past centuries as they are contains varieties of nutrition rich compounds such as carbohydrates, lipids, fat, proteins, fibers, vitamins and minerals (Mustafa *et al.*, 2018). The mycelium and fruiting body consists a wide range of metabolites with biologically active components that helps them to survive in adverse conditions by competing with other organisms for and nutritions and growth (Sharareh *et al*., 2016). Those bioactive compounds inhibits the other organisms with the production of antimicrobial components like antibiotics, antiparasitic and insecticides etc.(Anja and Timm 2009) and also have antifungal, antiviral, antioxidant, anticancer, anti-inflammatory and immunomodulation properties (Mustafa *et al.*,2018).

A numbers of global population having various health problems and diseases (Jyoti *et al.*, 2016) and so many natural, synthetic and semi- synthetic antimicrobial agents have been developed in previous century to treat varieties of diseases (Mehmet *et al*., 2009). At present situation microbial resistance towards first line and second line drugs has been increased drastically and its being very difficult to treat infections and diseases (Alves *et al.*, 2010).This demands caused the rise of finding different bioactive natural antimicrobial compounds from natural sources like plants, mushrooms and others (Mehmet *et al*.,2009). Pharmaceutical industries is looking for various natural sources of bioactive compounds with different biological properties for the production of antibiotics (Magdalena *et al.*, 2013).

A large no of enzymes and secondary metabolites are produced by white rot fungi have high therapeutic and medicinal values (Gebreselema *et al*., 2019, Mohammed *et al*., 2015). Those bioactive compounds such as cellular components and other metabolites are different in molecular weight such as phenolic compounds, high molecular weight polysaccharides, proteins, glycoproteins and tocopherols have shown antimicrobial and antioxidant activities in some isolated higher macro-fungi. Some authors have identified some secondary metabolites such as terpenoids, polyphenols, sterols, flavonoids, alkaloids, benzoic acid derivatives, quinolones, anthraquinones , lactones etc.(Magdalena *et al*., 2013). Some authors have mentioned that the phenols and flavonoids derivatives have the strongest antioxidant and antimicrobial properties among all metabolites (Magdalena *et al*., 2013, Srikram *et al*., 2016). White rot fungal metabolites have potential industrial, agricultural, environmental and biotechnological applications in production of pharmaceutical products.

Such as in pulp industries such as bioleaching of pulp, in paper industries, waste water treatment, degradation and transformation of environmental pollutants, improvement of cellulose and lignin digestibility in animal, production of renewable raw materials from lignocellulosic materials, in bioremediation and bioaugmentation technology, agricultural wastes revalorization etc.(Ed de Jong 1993, Zhong and Xiao 2009, Jurado *et al*.,2011 and Rodríguez-Couto S 2012).

The purpose of the study is to find out different types of bioactive white rot fungal metabolites produced during their growth phases, their antimicrobial activities and nutraceutical properties with respect to the human health specially the disease control properties. Various literatures and studies on white rot fungi have mentioned the functions of primary and secondary metabolites and they could make some contribution in various biomedical researches and in the development of new pharmaceutical products and drugs discovery is a major challenge now a days from novel bioactive metabolites of white rot fungi.

II. RANGE OF METABOLITES PRODUCED BY WHITE ROT FUNGI:

. Metabolism is a biochemical process by which all the life processes are accomplished and it's a fundamental process for all cellular life form (Thirumurugan *et al*., 2018). White Rot Fungi are one of the most beneficial organism on Earth due to the abilities of synthesizing numerous number of bioactive metabolites like other organisms (Magdalena *et al*., 2013).

Mycelial structure and the fruiting bodies produces a vast number of metabolites having unique biological properties and functions that helps them to survive in nature (Anja and Timm 2009, Jiang and Jie 2004). Their metabolites can be classified into two categories are,

Primary metabolites of white rot fungi are produced by different cellular metabolisms during the growth phase and development(Sanchez and Demain,2008). The products of primary metabolisms are used as building blocks for the production of potential biomolecules are amino acids and peptides such as phenyl alanine and tyrosine and leucine, valine, glycine(Lapadatescu *et al*., 2000, H. C Beck 1997, Moore *et al*., 2020 and Stergiopoulos *et al*., 2013), nucleotides ,organic acids such as oxalic acid, acetic acid, citric acid and malonic acids (Dashtban et al., 2010, Sanchez and Demain 2008), carbohydrates and polysaccharides such as glucose, xylose, galactose, mannose and arabinose etc.(Hatakka and Hammel 2011)

Vitamins such as tocopherols(Magdalena *et al*., 2013), different extracellular and hydrolytic enzymes such as pectinase, chitinase, cellulase and xylanase, manganese peroxidase, lignin peroxides and laccase (Fonseca *et al*., 2015, Alves *et al*., 2010, Rabha and Dhruva, 2018, Chin-Han Shu 2007) alcohol such as ethanol, benzyl alcohol and vanillyl alcohol (Lapadatescu *et al*., 2000, Mattila *et al*., 2020, Dashtban *et al*., 2010).

Secondary metabolites are produced by using the intermediate or by-products of primary metabolisms in certain growth periods (Keller *et al*., 2005). Secondary metabolites are not very much essential for growth and development but they possess different biological properties such as antimicrobial, anti-parasites, insecticides, signaling molecules in microbial interactions, such as competition and symbiosis as they are saprophytic in nature (Thirumurugan *et al*., 2018, Anja and Timm, 2009).
Important types of secondary metabolites are Terpenoids such as Taxol, lanosterol, pleuromutilin and illudin, ganoderic acid, hirsutane and ergosterols etc.(Kuhnert *et al*., 2018, Deepak and Deepika, 2015, Anja and Timm, 2009).

Sterols, Phenols and phenolic compounds such as flavonoids, lignans, quinones, tannins, coumarins, gallic acid, para-hydroxybenzoic, ferulic acid, syringic acid, Tyrosol and hydroquinone (Gan *et al*., 2019, Jing Xu , 2010, Monika *et al*., 2017, Ramon and Janet 2020), Polyketides, Alkaloids and fatty acid such as sterenins, orsellinic acid, Pestalachloride, Terphenyl, and Strobilurin (Mengqing *et al*., 2020, Jing Xu 2010, Risa *et al*.,2018), non-ribosomal peptides etc.(Kaller *et al*., 2005).

Carbohydrates and Polysaccharides such as β-d-glucans, glucose, mannose, galactose(Wang et al.,2017, Vladimir Elisashvili 2012, Hatakka and Hammel, 2011), Proteins and Glycoproteins such as lectins, pectin, heme peroxidase like manganese, lignin and versatile peroxidase, anthraquinones etc.(Dashtban *et al*., 2010, Magdalena *et al*., 2013, Thirumurugan *et al*., 2018 Anja and Timm 2009, Jing Xu *et al*.,2010).

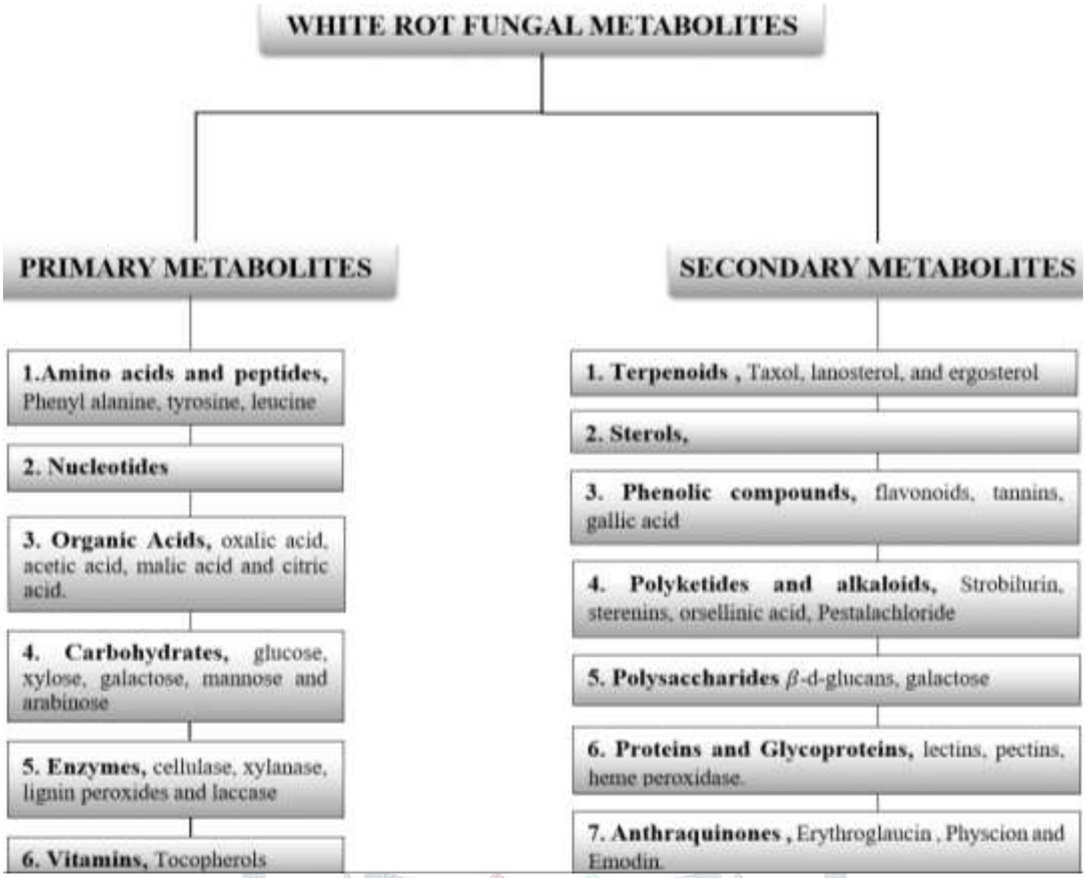

Figure 1- Types of white rot fungal metabolites

III. BIOSYNTHETIC PATHWAYS INVOLVED IN SECONDARY METABOLITE PRODUCTION BY WHITE ROT FUNGI:

For the commercial production of secondary metabolites some important parameters are the addition of nutritions, environments and the conditions of culture promotes the biosynthesis of secondary metabolites fermentation (Bills *et al*., 2008, Moreira *et al*., 2003) and some conditions such as aeration in a liquid culture, oxygen requires, conditions of temperatures, growth mediums substrates, and antifoaming agents added onto the fermenter where a little variations in the parameters can effect on the quantity, nature and diversity of the fermented products or metabolites (Barberel & Walker 2000, Magdalena *et al*., 2013, Moreira *et al*., 2003).Various chemicals or substrates which are used generally transformed by the actions of cellular enzymes in metabolic pathways and the production of bioactive metabolites used as building blocks for production of secondary metabolites containing varieties of mechanisms (Jens Christian Nielsen, 2018).

A study was done with a polycyclic aromatic hydrocarbon or PAH, Phenanthrene was added to a medium with the growth of the white rot fungus *Pleurotus ostreatus* and *Ganoderma lucidum* metabolized the PAH by various metabolic pathways involving various enzymes to form some compounds such as phenanthrene cis-dihydrodiol and trans-dihydrodiol, protocatechuic acid or catechol, 2,2-diphenic acid and unidentified metabolites (Bezalel *et al*., 1996, Agrawal *et al*., 2018). Various enzymes are involving in the degradations of various compounds and results in the formations of biproducts of cellular metabolism(Goyal *et al*.,2016, Agrawal *et al*., 2018, Bezalel *et al*., 1996).

Secondary metabolites are the end products of cellular metabolisms are produced by using the products of primary metabolism as building blocks (Christina Nord, 2014). They are well known bioactive compounds with structural diversity and are synthesized by various metabolic pathways combinedly are basically named from the action of enzymes or any intermediates are involved in cellular metabolisms (Goyal *et al*.,2016).

Common biosynthesis pathways are,

a. The mevalonic acid pathway synthesis of terpenoids, steroids etc
b. The shikimic acid pathway synthesis of aromatic amino acids, alkaloids
c. The acetate pathway synthesis of polyketides, fatty acids and non-ribosomal peptides
d. Synthesis of carbohydrates and polysaccharides

1. THE MEVALONIC ACID PATHWAY:

Tit is a common pathway of many plants and fungi including white rot fungi and he fundamental building blocks of the mevalonic acid pathways are dimethylallyl diphosphate and isopentenyl diphosphate (David Hansson, 2013).Terpenes, steroids are secondary metabolite of white rot fungi can be synthesized in mevalonic acid pathway that is a common pathway of integration of the primary and secondary metabolic products (Kaller *et al*., 2005, Thirumurugan *et al*., 2018 and Goyal *et al*., 2016). Examples of terpenes metabolites are sesquiterpenoid, diterpenoids and triterpenoids are produced in this pathway. White rot fungi mostly follows this mevalonic acid pathway for the synthesis of terpenoids (David Hansson, 2013).

2. THE SHIKIMIC ACID PATHWAY:

The shikimic acid pathway is an biosynthesis pathway of white rot fungi for the production of various aromatic amino acids and compounds such as acids L-phenylalanine, L-tryptophan and L-tyrosine, glycine, various proteins and sterols etc (Goyal *et al*., 2016, Moore et al., 2020). The Initiation of shikimic acid pathway occurred by the participation of Phospho-enol pyruvate and erythrose 4-phosphate are two important intermediate compounds of carbohydrate metabolisms to produce the shikimic acid .Then Shikimic acid is phosphorylated with another Phospho-enol pyruvate molecules and attached to another group of shikimic acid. The sequential elimination of the phosphoric acid leads to the end product of shikimic acid pathway and helps in the formation of many other important compounds followed by the process of decarboxylation and aromatic amino acids are formed and results in the production of amino acids in this pathway (Goyal *et al*., 2016, David Hansson, 2013). Benzoic acid derivates and phenolic compounds are originated from this pathway and Tannic acid is formed by the reaction of glucose and shikimic acids following shikimic acid pathway (Nowicka and Kruk, 2010, Thirumurugan *et al*., 2018).

3. THE ACETATE PATHWAY:

The Fungal polyketides are generally synthesized by polyketide synthases or PKs are composed of a multi domain proteins and non-ribosomal peptides synthase or NRPs by following the PK and NRP pathways (Kaller *et al*.,2005, Jens Christian Nielsen, 2018, Vito Valiante 2017). These enzymes contain short chains of carboxylic acids such as acetyl CoA and malonyl Co-A are two important products of tri carboxylic acid or TCA cycle is involved in polyketide and fatty acid synthesis, those compounds are produced by acetic acid pathway and the β oxidation of fatty acids(Moore *et al*., 2020, Kaller *et al*., 2005, Collemare and seid 2019). Polyketide synthase simulates the decarboxylation reaction and other intermolecular reactions and anthraquinones can be synthesized in this pathway (David Hansson, 2013, Nowicka & Kruk, 2010).

5. SYNTHESIS OF CARBOHYDRATES AND POLYSACCHARIDES:

The biosynthetic pathways of carbohydrate are identical and common in most white rot fungal species in compared with the other saprotrophic fungus (Deveau *et al*., 2008). Polysaccharides are the long chain of carbohydrates molecules are joined together with galactosidase bonds are essential components for all living organisms and important components produced by primary metabolism and secondary metabolism (David Hansson, 2013, Kaller *et al*.,2005). Carbohydrates and polysaccharides such as glucose, mannose, galactose and glucan are produced via several reverse pathways are like glycolytic, gluconeogenesis, pentose phosphate pathway and krebs cycle or tricarboxylic acid cycle from non- carbohydrate sources (JW Deacon 2013 and Deveau *et al.*, 2008).

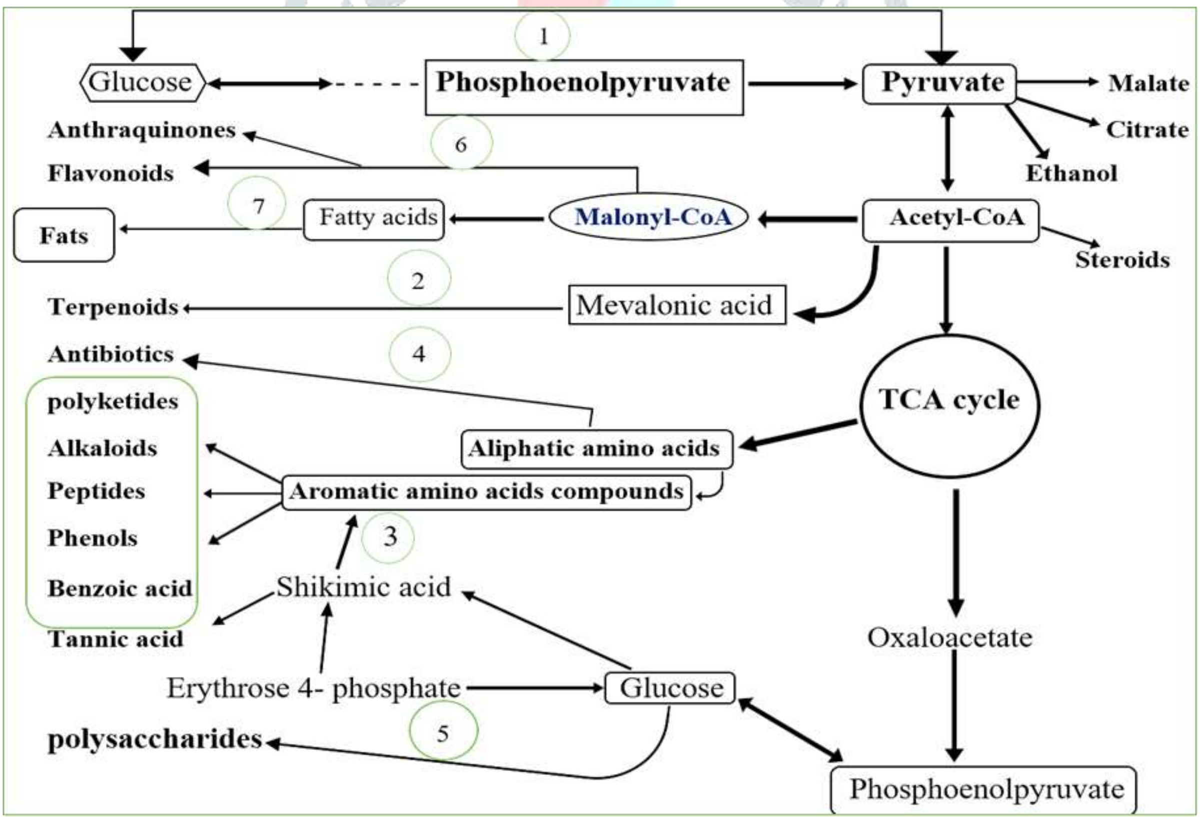

Figure -3. Over all biosynthetic pathways of primary and secondary metabolism. 1. Glycolytic pathway, 2. Mevalonic acid pathway, 3. Shikimic acid pathway, 4. Amino acid derived pathway, 5. Glucose derived pathway, 6, 7. Acetate Pathway and β oxidation of fatty acids.

IV. SIGNIFICANCE AND APPLICATION OF SECONDARY METABOLITES PRODUCED BY WHITE ROT FUNGI :

White rot fungi is an abundant source of metabolites, in which mycelium and fruiting bodies produces a varieties of biomolecules with biologically properties (Gaoxing *et al*., 2018,Magdalena *et al*., 2013) are turning the attention of researchers for the potential applications of the bioactive metabolic compounds, such examples many researches and studies have been done by using the compounds in various area such as in industries like pulp and paper industries, pharmaceutical industries, in agricultural waste degradations, environmental applications such as bioremediation and biotechnological applications, waste water treatment etc.(Ed de Jong 1993 and Zhong and Xiao 2009).

I. TERPENOIDS :

An intrinsic ability of white rot fungi is to the production of terpenoids, is an important and potential compounds among all other classes of secondary metabolites (Hirofumi and Takuya 2018). Previously it was thought to be produced by plants and some Actinomycetes but at present various investigations have revealed that it also produced by some species of white rot fungi a group of wood decaying basidiomycetes (Anja and Timm 2009). Three important types of terpenes are sesquiterpenoid, diterpenoids and triterpenoids are structurally and functionally different and represents an interesting biological activities(Deepak and Deepika 2015). Terpenoids are produced by some white rot fungal species are, Cortinarius herculeus, Cystoderma Carcharias, Cystoderma amianthinum, Conocybe sp, Pestalotiopsis spp, Ganoderma lucidum etc (Anja and Timm 2009, Jing Xu 2010, Deepak and Deepika 2015).

3.2 SESQUITERPENOIDS:

Sesquiterpenoids consists of wide varieties of structural derivatives having different and unique functional properties and it has various subtypes such as hirsutane, norilludalane, isolactarane, illudalane, stereumane, cadinane, sterpurane, drimane are isolated from a wood decaying white rot fungi Stereum spp.(Mengqing et al., 2020). β-eudesmane and β-eudesmol are produced by Polyporus brumalis(Lee *et al*., 2016) Illudane, illudalane and protoilludane are derived from Clitocybe illudens and Gloeophyllum sp., Coprinol another sesquiterpenoid was isolated from a wood inhabiting white rot fungi Coprinus sp., illinitones A and B as well as limacellone were screened from Limacella illinita (Anja and Timm 2009, Deepak and Deepika 2015).

3.3 DITERPENOIDS:

Diterpenoids are not frequently found in all the species of white rot fungi but some species can produce this compounds (Anja and Timm 2009). It contains about 20 carbon atoms and has approximately 7000 derivatives (Fozia *et al*., 2018).Taxol is a well-known diterpenoids produced by wood rotting endophytic fungi such as Pestalotiopsis sp., that is biologically functional and its highly recommended in biomedical research (Jing Xu 2010). Another types of diterpenoids compounds are tintinnadiola and strobilurins drived from the mycelium and fruiting bodies of white rot fungi Mycena tintinnabulum (Deepak and Deepika 2015).

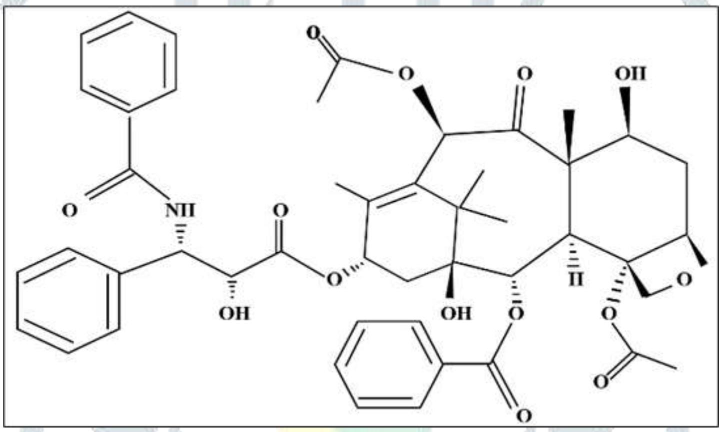

Figure 2- Structure of Terpenoid Taxol

3.4 TRITERPENOIDS:

Triterpenoids are another important class of terpenes and it is a naturally produced compounds and highly oxidized in structure (Deepak and Deepika 2015). Most of the white rot fungi along with all fungal metabolites are prolifically produces triterpenoids like Laschiatrion compound is produced by Favolaschia spp, fomitellic acids derivatives are derived from Fomitella fraxinea , clavaric acid produced by Clavariadelphus truncates and another triterpenoid derivative ergosterol isolated from Grifola frondosa (Anja and Timm 2009).

II. STEROLS:

Sterols are a predominant alcoholic secondary metabolites has been isolated from the white rot fungal species Stereum hirsutum (Mengqing *et al*., 2020). Steroids compounds are basically joined with each other by four cycloalkane rings (Deepak and Deepika 2015). Ergosterol is one of the important sterol compounds produced by some white rot fungi (Ellen Kandeler 2007). Esters of ergosterol are found in most of white rot fungal cells (Yaoita *et al*., 2015). Another example of sterol is secoergosterols with structural derivatives have been isolated from the fruiting bodies of the white rot fungal species Tylopilus plumbeoviolaceus (Deepak and Deepika 2015). Some other novel sterols compounds also found in Stereum hirsutum are isocyathisterol, ergosterol peroxide, Epidioxysterols and isocyathisterol (Mengqing *et al*., 2020).

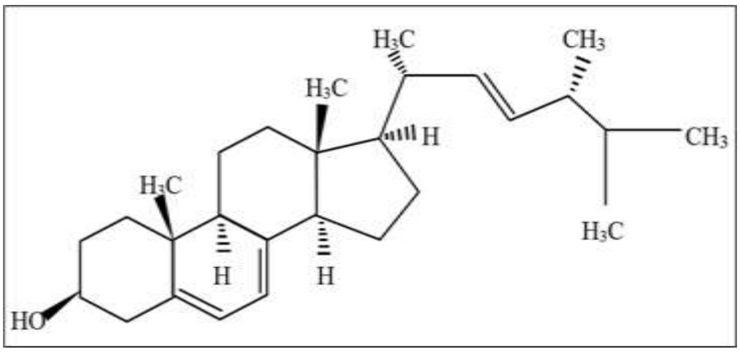

Figure 3- Structure of Ergosterol

III. PHENOLS AND PHENOLIC COMPOUNDS:

The Phenols and phenolic compounds are a group of small molecules containing of phenol units those are combined in a chemical structure are called phenolic compounds and it has various types of derivatives such as flavonoids, lignans, quinones, tannins, coumarins, p-hydroxybenzoic and curcuminoids protocatechuic(Gan *et al*., 2019). Phenols are one of the intrinsic secondary metabolites produced by the most of the plants and higher fungi basidiomycetes like white rot fungi (Ramon and Janet 2020). This compounds have high potential activities and therapeutic values among fungal metabolites (Jing Xu 2010). Phenolic acid compounds are produced inside of the cells cellular biosynthesis pathways of white rot fungi such as Ampelomyces sp, Phoma pinodella, Pestalotiopsis sp (Ramon and Janet 2020). Tyrosol, is an example of phenolic compound that has been isolated from the extracts of Pestalotiopsis sp (Jing Xu 2010) another phenolic compounds are gallic acid, ferulic acid, syringic acid found from some white rot fungal species (Monika *et al*., 2017). The Phenolic and flavonoid compounds are considered as a very significant constituents with antioxidant properties of such derivatives are rutin, phlorizin, gallic acid, quinone, 2,6-di-tert-butyl hydroquinone, vanillyl alcohol, catechol, guaiacol, acteosyringone and syringic acid (Dashtban et al., 2010, Ramon and Janet 2020). Many of phenol derivatives like, 4-(2-hydroxyethyl)phenol , 4-hydroxybenzaldehyde and 2-(2-hydroxyethyl)-4-methoxyphenol were isolated from the secondary metabolites of Stereum sp(Mengqing *et al*., 2020).

IV. POLYKETIDES, ALKALOIDS AND FATTY ACID DERIVATIVES:

White rot fungi are well known for producing alkaloids and polyketides and fatty acid derivatives (Deepak and Deepika,2015) produced by cellular metabolic pathways and They are considered as a large group of secondary metabolites (Mengqing *et al*., 2020). These are the natural products having therapeutic potentials and for this reason many pharmaceutical products are thought to be manufactured by using polyketides, alkaloids and fatty acid derivatives (Deepak and Deepika, 2015).

Examples of alkaloid derivatives such as sterenins, orsellinic acid isolated from Stereum sp., a chlorinated benzophenone alkaloid Pestalachloride is derived from Pestalotiopsis adusta (Mengqing *et al*., 2020, Jing Xu, 2010). Terphenyl is a alkaloid pigment is isolated from shikimate acid pathway from Thelephora sp., another derivatives such as Suillumide is isolated from the fruiting bodies of Suillus luteus. An alkylitaconic acid is ceriporic acid is derived from a white rot fungal species Ceriporia subvermispora (Anja and Timm,2009). Strobilurin a known polyketide compounds are produced by various species of white rot fungi such as Strobilurus tenacellus (Risa *et al*., 2018).

V. POLYSACCHARIDES:

Polysaccharides are well known white rot fungal bioactive metabolites have been derived from the fruiting bodies of white rot fungi with biological properties such as medicinal properties (Deepak and Deepika, 2015) such as antitumor, anti-inflammatory, hypoglycemic activities, antiviral, antioxidative etc. (Wang *et al*.,2017, Rajasekar et al., 2008). These biomolecules are composed of polymers of monosaccharide residues are linked together by α or β glycosidic bonds(Rajasekar et al., 2008). High molecular weight polysaccharide β-d-glucan and monosaccharides glucan are produced by white rot fungal species such as Stereum sp., Ganoderan sp., Phlebia radiata, Schizophyllan sp., Lentinan sp., Grifolan sp. etc. (Wang *et al*.,2017, Rajasekar et al., 2008). Some extra cellular polysaccharides are produced from white rot fungal species Schizophyllum commune, Pycnoporus sanguineus, Trametes villosa and Phellinus sp. (Vladimir Elisashvili 2012 , Monika *et al*., 2015).

VI. PROTEINS AND GLYCOPROTEINS:

A large number of polypeptides and glycoproteins are derived from white rot fungal species (Anja and Timm, 2009). Glycoproteins compounds are basically composed of oligosaccharides called glycans and are covalently joined with the poly peptide side-chain and an example of glycoprotein is lectins is isolated from Tricholoma Mongolicum, Phallus sp., Lactarius sp., Russula sp (Deepak and Deepika, 2015, Vladimir Elisashvili, 2012). Other glycoproteins produced by white rot fungus are pectin, manganese, lignin and versatile peroxidase are the type of glycoproteins are typically called as heme peroxidase composed with heme group of proteins with oligosaccharides produced by Phanerochaete chrysosporium and Trametes versicolor(Dashtban *et al*., 2010). It is a heterogeneous carbohydrates binding protein that participates in various cellular mechanisms such as cell to cell adhesions, cells recognition, cell differentiation, sugars transports and in growth regulation (Vladimir Elisashvili, 2012).

VII . ANTHRAQUINONES:

Anthraquinone is a secondary metabolites produced few white rot fungal basidiomycetes of the genus Lentinus sp. is generally uncommon metabolites also has antimicrobial properties (Bartholomeu *et al*., 2012). It has structural varieties among them eight of anthraquinone derivatives were also reported are 6-Methylxanthopurpurin-3-O-methyl ether, austrocortirubin, austrocortilutein, austrocortilutein and torosachrysone isolated from the white rot fungal species Cortinarius basirubencens, and Erythroglaucin, Physcion and Emodin has been isolated from Cortinarius sp.(Maria *et al*., 2012).

V. IMPORTANCE OF SECONDARY METABOLITES OF WHITE ROT FUNGUS WITH RESPECT TO HUMAN HEALTH:

White rot fungi is a wood decaying fungi a group of basidiomycetes also called as mushroom (Jennison *et al*., 1957). Since historical times it has been consumed as food and the people of the ancient Greek used to belief that it was responsible for providing strengths and used as food sources and was called "Food of the Gods"(Folman *et al*., 200). From previous centuries its being cultivated and consumed as nutritional foods in China (Deepak and Deepika 2015).

The fruiting bodies of white rot fungi contains a large number of pharmacological active compounds with medicinal features with respect human health(Vivek *et al*., 2018).

NUTRACEUTICAL BENEFITS:

From the past several years the consumption of white rot fungi as food supplement has increased due to the nutraceutical benefits with aroma, texture and flavors as well as the ability of preventing several diseases (Heleno *et al*., 2015). Some specific white rot fungal species are Agaricus campestris , Lentinula edodes, Cyclocybe aegerita, Pleurotus sp.(Titas *et al*., 2019) composed of high content of dietary fibers, water composition, low fat and low-calorie protein content including the essential amino acids along with numerous no of minerals and vitamins B12 or riboflavin, B3, B5 and vitamin C and D, Copper, Selenium, Potassium, carbohydrates and nitrogen rich compounds, lipids etc.(Mustafa Sevindik, 2018, Gaoxing *et al*., 2018 , Titas *et al*., 2019). Various studies has shown that the bioactive compounds have medicinal and therapeutic properties such as anti-diabetic, anti-oxidants, anticancer, antimicrobial agents, immunomodulatory properties, anti-obesity, hypocholesteremia and anti-aging along with the less in hypertensions and stress factors in human body (Vivek *et al*., 2018, Gaoxing *et al* ., 2018 Tolera *et al*., 2017).The nutraceutical bioactive compounds have showed quite effective with respect to human health and diseases are polysaccharides, proteins, glycoproteins, unsaturated fatty acids , phenolic compounds, tocopherols, ergosterols, lectins etc.(Gaoxing *et al*., 2018).

ANTIMICROBIAL PROPERTIES OF WHITE ROT FUNGI AGAINST PATHOGENIC MICROBES:

Numerous no of investigations have been done with different bioactive molecules obtained from white rot fungi by different screening methods and the studies revealed that white rot fungi could be an alternative and natural source of bioactive compounds with medicinal properties (Gaoxing *et al*., 2018) such as, antimicrobial, antiviral, antioxidant, anticancer, anti-inflammatory and immunomodulatory properties, antitumor, anti-diabatic, hypoglycemic, neurotrophic, cytotoxic and hepatoprotective effects (Wang *et al*.,2017, Xiao and Zhong, 2016 and Mustafa *et al*.,2018).

In a study three bioactive fractions of white rot fungal species such as extracellular laccase, crude-endo-polysaccharides, and extracellular low molecular weight subfractions were investigated their antioxidants and antimicrobial potential from metabolites. Three bioactive compounds were was studied with different assay such as determination of carbohydrates, proteins, phenolic compounds, ABTS radical-scavenging assay and DPPH free radical-scavenging antioxidant assay, and then antibacterial activities were done with the fractions against bacteria Escherichia coli, Staphylococcus aureus are pathogen to human. Among the three bioactive fractions ex-LMS, and C-EPL showed highest antimicrobial and antioxidant properties (Magdalena *et al*.,2013).

Some authors collected some wild rot fungi from different sources for their studies and metabolites screening where antibacterial activity was done with different mycelium crude extracts against pathogens in well diffusion and minimum inhibitory concentration method on Muller-Hinton Agar and broth (Jyoti *et al*.,2017, Tsungai *et al*.,2016).

The phytochemical activities are done by various methods and it has been observed that hot water metabolites extracts showed highest antimicrobial activities against pathogenic microorganism and flavonoid and phenol derivatives showed highest antioxidant properties and are one of the natural sources of antibiotics and can be used as the natural antimicrobial agents for the production of new drugs for the treatments of bacterial infections (Jyoti *et al*., 2017).

On another study antimicrobial activities were checked of a white rot fungal species Pleurotus ostreatus and identified that the compounds acted against pathogenic organisms such as Staphylococcus aureus, Escherichia coli. Candida albicans and Cryptococcus humicola and then the components were further purified by thin layer chromatography and NMR spectrometer and mass spectroscopy methods and it has been concluded that the mycelium extract showed a broad spectrum antimicrobial activity and authors have concluded that the mycelial extracts contains medicinal compounds that could be used as medicinal products to fight against infectious disease (Ahmed *et al*.,2015).

In a study seven species of white rot fungi were Grifola frondosa, two species of Polyporus sp., Pleurotus sajorcaju, Pleurotus florida, Schizophyllum commune and Jelly sp. were used to screened for the production of exopolysaccharides having antimicrobial properties that could be used in pharmaceutical industries (Yogita *et al*.,2011). A white rot fungal strain of Hypholoma fasciculare a wood decomposer fungus have investigated for the antibacterial activities and the metabolites produced by white rot fungi showed less effective but it has the capability of acting against bacterial infections (Boer *et al*.,2010).

Another studied showed some antimicrobial activities of a white rot fungal metabolites against pathogenic microorganisms and the novel antimicrobial components by white rot fungus is a natural source of antimicrobial agents (Mehmet *et al*.,2009).

A study was done by collecting the fruiting bodies of two white rot fungi from a forest of Sri Lanka to investigate the antioxidant properties of different bioactive fractions from white rot fungal species because white rot fungus possess a great variety of metabolites with polyphenolic substances and from their studies they have found that bioactive compound such as phenols and phenolic compounds have strong antioxidative potential that could be used to treat many kind of diseases such as cancer, tumor's, aging, cardiovascular disease , atherosclerosis etc.(Muthuthanthriege *et al*.,2019).

A study on human epithelial cells and cancer cells were done by using the extracellular fractions of a white rot fungal species and investigated their therapeutic properties. Antioxidant and anti-cancer assays were done and analyzed by FT-IR spectroscopy to determine the inhibitory mechanisms of extracellular bioactive fraction towards cancer cells and their analysis showed that the bioactive extracellular fractions can be used to treat colon cancer that is one of the lethal cancer Worldwide (Anna *et al*., 2019).

Table 1. Different bioactive compounds and their functions of white rot fungi :

Bioactive compounds	**Name of the sources White rot fungal species**	**Biological functions**	**References**
Terpenoids	*Cortinarius herculeus,* *Cystoderma Carcharias* *Cystoderma amianthinum* *Conocybe sp* *Pestalotiopsis spp* *Ganoderma lucidum*	Flavours and odor with anti-infectious and anti-inflammatory activities	Deepak and Deepika 2015, Anja and Timm 2009
Sesquiterpenoid	*Stereum hirsutum* *Ripartites sp.* *Clitocybe illudens* *Gloeophyllum* *Coprinus sp.* *Limacella illinita*	Antitumor, antimicrobial cytotoxic activity, acts as novel fungicide, antibacterial activities, Nematicidal activities inhibits The aggregation of human thrombocytes, acts against gram positive antibiotic resistance bacterial strain such as methicillin resistant *staphylococcus aureus.*	Xiao and Zhong, 2016 Anja and Timm, 2009 Deepak and Deepika,2015.

Diterpenoids	*Mycena tintinnabulum* *Sarcodon scabrosus* *Cyathus africanus* *Clitopilus passeckerianus*	Antimicrobial Anti-inflammatory and Anticancer Neurotrophic and cytotoxic activity	Fozia *et al*., 2018 Jing Xu,2010 Deepak and Deepika,2015 Xiao and Zhong, 2016
Triterpenoids	*Favolaschia spp* *Fomitella fraxinea* *Clavariadelphus truncates* *Grifola frondosa* *Ganoderma lucidum* *Naematoloma fasciculare*	Antitumor, anti-HIV, Antimicrobial, Antioxidant properties, Antitumor , Antifungal activity, Cytotoxic activities towards the human cell lines A549 in case of lung carcinoma , and CAKI 1 in case of human kidney carcinoma , and in Hep-G2 that is human liver carcinoma.	Anja and Timm,2009 Deepak and Deepika, 2015 Xiao and Zhong, 2016
Phenolic compounds and flavonoids	*Ampelomyces* sp. *Phoma pinodella* *Pestalotiopsis* sp. *Agaricus* sp. *Stereum sp.*	Antioxidant activities oxidative stress reduction, Antimicrobial activities against Staphylococcus pathogenic bacteria, Cytotoxic activities , Scavenging activities of DPPH free radicals in the human body.	Deepak and Deepika,2015 Magdalena *et al*., 2013 Ramon and Janet, 2020
Polyketides, Alkaloids and Fatty Acid Derivatives	*Stereum* sp. *Pestalotiopsis adusta* *Suillus luteus* *Ceriporia subvermispora* *Strobilurus tenacellus*	Antibiotic, Antifungal, Anticancer, Hypolipidemic, Immunosuppressive properties	Anja and Timm,2009 Risa *et al*.,2018 Deepak and Deepika, 2015 Mengqing *et al*., 2020 Jing Xu, 2010
Sterols	*Stereum hirsutum* *Tylopilus plumbeoviolaceus* *Lentinula edodes* *Cordyceps sinensis* *Tricholomopsis rutilans*	Acts against to both Gram positive and Gram negative bacteria, Antioxidative properties	Ellen Kandeler, 2007 Mengqing *et al*., 2020 Deepak and Deepika, 2015
Glycoproteins	*Agaricus campestris* *Tricholoma Mongolicum* *Phallus* sp. *Lactarius* sp. *Russula* sp.	Various cellular mechanism like Cell to cell adhesions , Cells Recognition , Cell Differentiation, Glucose Transports Growth regulation in living organisms	Anja and Timm, 2009 Vladimir Elisashvili, 2012 Deepak and Deepika, 2015
Polysaccharides	*Stereum* sp. *Ganoderan* sp. *Lentinan* sp. *Grifolan* sp. *Pycnoporus sanguineus,* *Schizophyllan commune* *Trametes villosa*	Anti- Cancer Anti-Tumor, Immuno-Modulatory Properties, Antiviral Activities, Antimicrobial Properties, Anti-Inflammatory, Hypoglycaemic Activities, , Antioxidative, Hepatoprotective Effects	Rajasekar *et al*., 2008 Wang *et al*.,2017 Mengqing *et al*., 2020 Monika *et al*.,2015 Vladimir Elisashvili 2012 Deepak and Deepika 2015
Anthraquinones	*Lentinus* sp. *Cortinarius basirubencens* *Cortinarius* sp.	Antimicrobial properties, Antioxidant activities.	Maria *et al*., 2012 Bartholomeu *et al*., 2012

VI. CONCLUSIONS :

From the study of the finding different bioactive compounds produced by white rot fungi a group of basidiomycetes, it has been observed that white rot fungi produces varieties of metabolites and composed of various nutrition rich compounds and for this white rot fungi is being considered as functional food supplements. Beside nutritional properties they have significant therapeutic values against infections and disease with respect to human health. They heterotrophic fungus considered as the natural sources of antimicrobial components. Various authors have studied and screened different white rot macro fungal species mainly focusing on to the medicinal properties and most of authors have concluded white rot fungi is a natural origin and biological sources of antibiotics that can be used as alternative source in pharmaceutical industries as well as biomedical research. We also found different biological active metabolites of white rot fungus, their metabolic pathways and then their nutritional components as well as medicinal components and the functions of each components towards human health and disease , it has been concluded that white rot fungi will lead to the contribution in pharmacological and nutritional researches field.

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CONFLICT OF INTEREST:
I declare of no conflict of interest.

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