MULTIDRUG-RESISTANT ORGANISMS: ANTIBACTERIAL ACTIVITY AND DRUG RESISTANT

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ABSTRACT

The continuous rise in antimicrobial resistance has led to an unending search for new, cheaper, and safer sources of antimicrobials. Antibiotic resistance is a challenging health problem that can't be over looked in the coming years. Considering that little advancement has been made in the discovery of antibiotics especially those effective against drug-resistant strains, use of alternative methods could be the best way to resolve this problem. Mushrooms are known to possess bioactive metabolites, which can serve as pharmaceutical agents. The antimicrobial activity of aqueous and methanol extracts from edible mushrooms *Pleurotus ostreatus* and *Agaricus bisporus* against four pathogenic bacterial strains; *Staphylococcus aureus, Bacillus subtilis, Escherichia coli,* and *Pseudomonas aeruginosa,* and the yeast *Candida albicans*were evaluated using the agar well diffusion method. This paper outlines the most frequent antibiotic-resistant bacteria and describes the advantageous and limitations of approach that have been proposed to control them.

Keywords: ***Antibiotic, antimicrobial resistance, mushroom. Agaricus bisporus***

1.0 INTRODUCTION

Developing worries about worldwide anti-toxin obstruction have dove into new profundities as the World Health Organization (WHO), is currently cautioning that the world is running out of anti-infection agents (WHO, 2020). The unremitting development of medication safe microscopic organisms has represented a basic test to the treatment of clinical sicknesses, bringing about a continuous expansion in the recurrence of unfavorable local area and nosocomial diseases. The quest and investigation for bioactive mixtures viable in treating pathogenic microorganisms impervious to introduce day drugs has become exceptionally extreme. By and by, there is a developing interest in looking for new antimicrobial specialists from regular sources like microscopic organisms, parasites, and plants. Mushrooms are meaty growths, fruiting bodies that bears spores which normally produce over the ground on soil or on their food sources which frames a significant gathering of more modest plant realm. Mushrooms are sufficiently enormous to be seen by the unaided eyes, they have unmistakable fruiting body, due to the nutritive substance, and a few mushrooms are eatable while some are used widely in customary prescriptions. Individuals have gathered wild mushrooms for medication and food sources for millennia. There are around 1200 known types of mushroom used in 85 divergent nations for their restorative properties (Wasser, 2014). Mushrooms have therapeutic properties particularly because of wealth in organically successful mixtures that have cancer prevention agent, antimicrobial properties reinforcing the insusceptible framework and guaranteeing against cancer-causing agents [1]. The utilization of manufactured medications has stayed an extraordinary worry to human wellbeing, in that it has various secondary effects which could likely prompt different illnesses and demise. Other report has it that a portion of these engineered anti-microbial medications could prompt instigated hepatoxicity, which would be more extreme in patients that are immunocompromised (Sharma et al., 2014). In progression, researchers presently lean toward the utilization of restorative plants, which incorporates mushrooms that have phytochemicals with antimicrobial exercises. Mushrooms, for example, Pleurotus ostreatus (Oyster) and Agaricus bisporus have been accounted for to have various medical advantages as: anticarcinogenic, calming, antitumor exercises. These bioactive mixtures are found in different cell parts and auxiliary metabolites, which have been confined and recognized from the fruiting bodies. The fruiting bodies and mycelium of mushrooms show wellbeing advancing qualities, for example, invulnerable stimulatory antibacterial, and antioxidative properties. While there is

a lesser lack of specialists dynamic against Staphylococci, the commonness of contaminations with methicillin-safe Staphylococcus aureus (MRSA) remains very high in numerous nations. Antimicrobial mixtures produced by green growth and organisms (mushrooms) against microbes have gotten extensive consideration as another wellspring of novel antimicrobial substances [2].

2.0 SPECIES OF ANTIBIOTIC-RESISTANT BACTERIAL

Medical services related contaminations raise grimness and death rates around the world. The increment in mortality is straightforwardly identified with antimicrobial obstruction which makes anti-microbial treatment more prohibitive, hence making it hard to treat diseases brought about by multiresistant microor-ganisms. Toward the start of the 21st century, diseases with carbapenem-safe gram-negative bacilli, mostly Enterobacteria, turned into a major general medical issue. [2]MDR gram-negative microbes including A. baumannii, Pseudomonas aerugionosa , expanded range beta-lactamase (ESBL)- delivering Enterobacteria, and carbapenem-safe En-terobacteria (CRE) are viewed as the vitally causative specialists of nosocomial contaminations. Methicillin-safe S. aureus (MRSA) and vancomycin-safe Enterococcus (VRE) have been accounted for as of late to be the most widely recognized bacterial microorganisms, what's more, medical clinics have likewise been segregated from food varieties of creature beginnings, water, and creatures. MDR P. aeruginosa, Carbapenem-safe En-terobacteriaceae, and A. baumannii have been basically asso-ciated with clinical examples, yet a few strains have likewise been separated from food varieties, creatures, and water. This multitude of strains have been related with deadly infec-tions, and in this part, their primary attributes will be tended to [3].

2.1 ANTIBIOTIC RESISTANCE APPROACH

The variety Acinetobacter comprises of gram-negative, high-impact cocobacillus that are universal, stationary, non-maturing, catalase positive, and oxidase negative. The A.calcoaceticus-A. baumannii complex is liable for the vast majority of the local area or clinic gained diseases [4]. The various types of Acinetobacter present in different normal environments can be confined from the dirt, water, vegetables, and creature and human hosts. They are important for the commensal vegetation of human skin and mucous films. A. baumannii can make due in an assortment of settings in the clinic climate: in dialysis machines, mechanical ventilation frameworks, water sources, skin and mucous films of wellbeing experts and patients, restorative arrangements, and sanitizers. For quite a while Acinetobacter was viewed as an astute specialist with low pathogenicity. In any case, the pres-ence of a few harmfulness factors that permit its endurance in the clinic climate and improve its ability to cause sickness have brought about it being one of the fundamental driver of nosocomial diseases in numerous countries[5]. As of late, the World Health Organization reported this microorganism as the main goal microbe, for which innovative work for new anti-toxins are earnestly required. A. baumannii is progressively embroiled for causing wellbeing related diseases, which give a high danger of horribleness and mortality to patients. This bacterium can likewise be exceptionally impervious to antimicrobials, particularly those iso-lated from the patients in the concentrated consideration units. Contaminations brought about by MDR A. baumannii strains might demolish patient results because of lacking introductory treatment, restricted treat-ment choices, and high poisonousness of accessible treatments. Hazard factors for contamination and colonization by MDR A. baumannii incorporate delayed hospitalization particularly in emergency unit, ventilation, focal venous catheteri-zation, urinary catheterization, past antimicrobial ex-posure, expanded infection seriousness, and openness to careful and obtrusive strategies [6]. This microorganism has logically amassed re-sistance to penicillins, cephalosporins, quinolones, and aminoglycosides. Thusly, carbapenems have turned into the treatment of decision for genuine diseases. The mecha-nisms of opposition of A. baumannii can be natural or ac-quired and are interceded by a few variables, like loss of layer penetrability and, all the more altogether, the supportive of duction of betalactamases, proteins that corrupt beta-lactam anti-toxins. Betalactamases are the main source of bacterial opposition, principally in gram-negative bacilli.. Protection from carbapenems may happen by joining various components, for example, change in the partiality to PBPs and efflux siphons. In any case, the principle types of protection from carbapenems are the statement of carbapenemases of gathering B and D of Ambler, metallo-b-lactamases, and OXA, separately [7].

2.2 MULTIDRUG-RESISTANT PSEUDOMONAS

P. aeruginosa is a nonfermenting gram-negative bacillus, generally dispersed in nature and in emergency clinic climate. Answerable for nosocomial diseases, it is one of the main sharp microbe causing circulatory system contamination, urinary lot contamination, and ventilator-related pneumonia, particularly in fundamentally sick patients getting concentrated consideration. Besides, it is additionally exceptionally impervious to many as of now utilized medications making it a significant general wellbeing concern [8].. P. aeruginosa is naturally impervious to

a few antimicrobials and has extraordinary adaptability to secure new qualities that give protection from numerous different medications. The anti-toxin opposition of this bacterium is basically because of the low cell divider porousness of this microorganism, which limits the up-take of anti-infection agents, related with wide obstruction instruments, for example, efflux siphons and catalysts, which alter or corrupt anti-microbials and drug targets. Carbapenems are typically important for the principal line of remedial decision for treatment of Multdrug-safe Pseudomonas (MDR) P. aeruginosa diseases. Protection from carbapenems happens predominantly because of the impermeability to the medication, loss of porin, and activity of efflux siphons, however the creation carbapenemases is the main system [9]. The principle carbapenemases communicated by P. aeruginosa are from class B of Ambler, called metallo- - lactamases (IMP,VIM, SPM, GIM, NDM, and SIM families). These proteins give protection from carbapenems and are encoded in plasmids and integrons of class 1, which are answerable for their fast worldwide spread by flat exchange. Aeruginosa impervious to carbapenems (PARC) has become one of the serious issues for clinics. Flare-ups of disease brought about by PARC have been accounted for by a few nations, including Brazil. The development of antimicrobial opposition is straightforwardly identified with an increment in the patients clinic stay, expanded hospitalization costs, and an expansion in the death rate. In PARC diseases, mortality might reach 53.6%.

3.0 ANTIMICROBIAL ACTIVITY

All test organisms used in this study displayed a high level of resistance towards 75% of the various mushroom extracts studied, with only the methanol extract of *P. ostreatus* displaying any inhibition against *B. subtilis* and *S. aureus*. The methanol extract of *P. ostreatus* at a concentration of 50mg/mL showed mean zone of growth inhibition of 8.00 ± 1.40 mm and 6.0±0.11against the Gram-positive Bacteria *B. subtilis* and *S. aureus* respectively. The lowest concentration observed to inhibit the sensitive *B. subtilis* is 12.5 mg/mL. At a value of $P < 0.05$, there is a strong significant difference between the mean IZD of the oyster methanol extract against *B. subtilis* when compared with the control drug ciprofloxacin. The P value was found to be 0.005731. Similarly, there is a significant difference in the mean IZD value obtain against *S. aureus* when compared with ciprofloxacin, with $P < 0.05$.

3.1 ANTIBODIES

The utilization of antibodies has additionally been proposed as a promising technique for the control of MDR bacterial strains, as they can improve phagocytosis or enactment of supplement proteins. To expand immunizer activity, a few creators have proposed the utilization of more than one isotype, for the most part a blend of Immunoglobulin M (IgM), Immunoglobulin G (IgG), and Immunoglobulin A (IgA). 127,128 A polyclonal arrangement improved with IgM immunoglobulins financially accessible is Pentaglobin (Biotest AG, Dreieich, Germany), which contains 76% IgG, 12% IgA, and 12% IgM (IgGAM). Until now, there are without a doubt three other authorized monoclonal antibodies items against irresistible targets: Palivizumab, Raxibacumab, and Panobacumab. A few examinations have shown the viability of this elective treatment, which is additionally quite possibly the most concentrated on method. [10] tried Panobacumab, a completely human monoclonal immune response of the IgM/K isotype coordinated against the lipopolysaccharide (LPS) O-polysaccharide moiety of P. aeruginosa, which upgrades the phagocytosis of this microorganism. The creators reasoned that this treatment is protected and is related with high clinical fix and endurance rates in patients creating nosocomial P. aeruginosa contamination. Shown that IgGAM initiates in vitro killing of MDR clinical segregates of K. pneumonia through improvement of phagocytosis. Results got by Giamarellos-Bourboulis. Additionally showed that IgGAM was successful as an extra to antimicrobial treatment for the administration of septic shock brought about by MDR gram-negative microorganisms. Diago-Navarro. 133observed that anticapsular antibodies advanced extracellular cycles killing, supplement affidavit, sending of neutrophil extracellular snares, and opsonophagocytosis of carbapenem-safe Klebsiella pneumonia. The creator inferred that the tried antibodies could eventually treat or ensure patients contaminated or in danger of disease by this MDR bacterium. Immune response forms with antimicrobial specialists have likewise been demonstrated to be powerful to control MDR strains by a few other authors.Verified that an antibodyantibiotic form wipes out intracellulars [11]. Aureus01 and this form was better than vancomycin for treatment of bacteraemia. Neutralizer coordinated photodynamic treatment was extremely successful in killing diverse MRSA strains, in all development stages and might be a decent contender for a clever treatment of MRSA contaminations. As expressed by Szijarto, aloof inoculation was a standard treatment choice in the preantibiotic time, and as we advance toward a potential postantibiotic period, it could be reasonable to rethink the benefits of this treatment. The genuine advances in the exploration and biopharmaceutical fabricating limits empower the

improvement of profoundly sanitized refined antibodies against a scope of pathogenic microorganisms. In addition, MAbs are coordinated against nonhuman targets and overall have a phenomenal security record. Like other elective strategies, antibodies can supplement anti-microbial treatment. A test of this treatment is to find atomic determinants of the microbes that are open on the cell surface [11].

3.2 EXTRACTION OF MUSHROOM CRUDE EXTRACTS

50g of each sample was weighed and successively extracted with 500 mL of 70% v/v methanol. The mixture was allowed to stand at room temperature (28 to 30°C) for three days with frequent agitation and homogenized. The supernatant was filtered using Whatman filter paper (number 1) (Sigma-Aldrich, Michigan, USA). The filtrates were concentrated in a rotary evaporator at 40°C under reduced pressure and lyophilized. The yield extracts were properly kept in air tight containers, labelled, and stored until required for use.

3.3 WARM AQUEOUS EXTRACTION

50g of each sample was weighed and transferred into 500 mL of boiled warm water (50 °C) in a beaker. The beaker was placed on a hot plate at 70 °C and allowed to stand for 4 hours with intermittent stirring. The samples were filtered using sieve cloth and centrifuged at 4500 rpm, for 30 minutes. The supernatants were conventionally heated to a final volume of 5 ml.

4.0 RESULT AND DISSCUSSION

Around the world, the frequencies of multidrug-safe organic entities are expanding and compromising the treatment of a developing number of both clinic and local area obtained irresistible illnesses. Accordingly, there is a dire requirement for the inquiry and improvement of new and powerful medications against current anti-microbial safe microorganisms. The utilization of normally sourced drugs has displayed promising impacts which has driven such countless researchers to make explores on regular sources particularly mushroom. Phytochemical mixtures like flavonoids, phenols, saponin, glycosides and tannins are viewed as significant optional metabolites in mushrooms. In this review, both the methanol and fluid concentrates of P. ostreatus and A. bisporus were completely found to contain alkaloids and glycoside. Mushrooms are viewed as non-wellsprings of flavonoids. The shortfall of flavonoids in mushrooms might be of organic benefit in their different natural specialties since these bioactive mixtures hinder exercises included their pigmentation, development and improvement. Parasitic species have been demonstrated to be extraordinary possible wellsprings of bioactive mixtures of high helpful worth. All test organic entities utilized in this review showed a significant degree of opposition towards 75% of the different mushroom extricates examined, with just the methanol concentrate of P. ostreatus showing any restraint against B. subtilis and S. aureus. The methanol concentrate of P. ostreatus at the most noteworthy grouping of 50mg/mL showed mean zone of development hindrance of 8.00 1.40 mm and 6.00.11against the Gram-positive Bacteria B. subtilis and S. aureus separately. Nonetheless, there is a solid critical contrast ($P < 0.05$) between the mean IZD of the P. ostreatus extricate against B. subtilis when contrasted and the control drug ciprofloxacin. Around 75% of the mushroom metabolites extricated in this review were not compelling in hindering development among Gram positive microscopic organisms. As per [1], antimicrobial exercises of mushrooms removes are incredibly affected by their natural surroundings which could prompt contrasts in the kind of auxiliary metabolites delivered and bioactive results. This is on the grounds that the environments and culture substrates, which are significant variables in the turn of events and creation of bioactive metabolites of the concentrated on mushrooms, are obscure. Different specialists have recently revealed the opposition of P. ostreatus separates by E. coli, S. aureus (Owaid et al., 2015; Akyuz et al., 2010). The growths separate (C. albicans) utilized in this review showed 100% protection from both methanol and watery concentrates of P. ostreatus and A. bisporus in this review. Essentially, (Akyuz et al. 2010), revealed no antifungal action of the concentrates of both P.ostreatus and A. bisporus against Candida albicans. There are a few different reports expressing the opposition displayed growths microbes towards muschroom removes, independent of the extraction strategies and solvents utilized (Gbolagade and Fasidi, 2005.. The antibacterial exercises against Gram positive microbes (S. aureus and B. subtilis) showed by the methanol concentrate of P. ostreatus signifies limited range action, and might be credited to the presence of other bioactive metabolites of different substance types in mushrooms compounds.

5.0 CONCLUSION

Antibiotic resistance is a challenging health problem that can't be over looked in the coming years. Considering that little advancement has been made in the discovery of

antibiotics especially those effective against drug-resistant strains, use of alternative methods could be the best way to resolve this problem. The extracts of *P. ostreatus* and *A. bisporus* prepared with methanol revealed potential antimicrobial activities against Gram positive bacteria (*S. aureus* and *B. subtilis*), with the best activity against *B. subtilis* (8.0±1.40). Globalization, excessive use of antibiotics in animal husbandry and aquaculture, use of multiple broad-spectrum agents, and lack of good antimicrobial stewardship can be listed as the factors most responsible for the spread of antibiotic resistance.

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