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Antibacterial aptitude: amid Metallic Nanoparticles, Plant extracts and Antibiotics

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ABSTRACT: Antibiotic resistance challenges the human scientific community to develop a master plan against pathetic eruption of bacterial pathogenic diseases. Microbes are regarded as, integral part of human society, especially bacteria, and play a key role in the food industry, textile industry and most of all pharmaceutical industries. With advancement in science, bacteria being ancient ancestors have developed smart mechanisms for their survival and escape from human interventions. History reveals, plant extracts and herbs were the first plan of action against bacterial strains, keeping the same mode of action, and the rise of antibiotics was enjoyed. After the development of synthetic antibiotics, blueprints of bacterial strains move towards progressing immunity or developing resistance against them.. Nanotechnology came into being and metallic nanoparticles despite nano size but extravagant properties devastate bacterial strains magnificently. Later, new approaches flourished with mingling antibiotics and nanoparticles as well as gene intonation along with the new scheme of mastery in microbiological assay. New strategies proved to be excellent bactericidal policy and no less than harbinger to treat diseases caused by virulent bacterial strains.

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Introduction

Microorganisms are promptly present in nature, in all our surroundings within our environment. Therefore, they play roles in contributing to spoilage of food and spread of diseases which can be chronic or temporary, fatal and superficial. What if suspiciously swab testing of a hand is done and thousands of microbes readily present...? Moreover, Testing for the recognition of microbes will be definitely the next point of action. Analyzing microbes for bactericidal and bacteriostatic approaches has become one major necessity. Amazing methods enable antibacterial activity and microbial pathogenicity of gram positive and gram-negative species of bacteria to be determined. Antibacterial activity detection is the most prevailing method reported by many researchers. Man is bound to use antibiotics even 3rd generation and medicinal plants and other herbal plants to cure diseases by utilization of some crude plant extracts but still effective results are not produced. This despair situation leads scientists to devise plans for complete blocking or killing of fatal bacterial strains for winning tug of war.

1. Nanotechnology and it's Antibacterial Potential

New technology has been involved in analyzing antibacterial activity and prove to be bactericidal with highly successful performance. This technology is employed by using metallic nanoparticles mainly. Nanotechnology has shaken up the world. As, materials and specially metals at 10^9 behave extra ordinary special with completely different properties. Currently, it has been used by researchers as a great substitute for antibiotics to combat against several antibiotic resistant bacteria (KS Bajwa et al., 2018). Nanotechnology is basically, the study of extremely microscopic size materials at unique size and remarkable effects and in collation antibiotics and medicinal plants are confronting with great zeal. Many metallic particles are known to contribute in this respect of fighting against bacterial activities but three of them have shown great potential of resistance.

Mode of action of metal nanoparticles

According to (Morones JR et al., 2005) three main effects caused by nanoparticles are:

1) smaller size ratio of nanoparticle rigorously disrupts the cell membrane functioning

2) penetration within bacteria causing damage to sulphur and phosphorus compounds mainly DNA

3) release of silver ions by nanoparticles can cause immense bactericidal effects.

It is claimed that gram negative bacteria show best results in comparison to gram positive bacteria against silver nanoparticles. This difference is

explained on the basis of the thickness of cell membranes of gram positive and gram-negative bacteria (Abbaszadegan A et al., 2015). Sondi I and Salopek-Sond were the first to revealed that silver nanoparticles create cavity and allow the aggregation of silver nanoparticles within the bacterial cell membrane topping up permeability and ultimately causing death (Sondi I, Salopek-Sondi., 2004). Moreover, the smaller the size of a nanoparticle, more destruction it will cause ... is the amazing fact revealed? In conformity with mechanisms reported by other researchers, (Brandelli A et al., 2017).

1.1 Antibacterial activity of silver nanoparticles

Historically, silver has sanitizing ability along with it, it has been used in unorthodox medicinal culture and culinary kitchen practices. It has been disclosed that silver shows surprising ability at nano-scale. SNPs are involved in many applications such as home appliances, household disinfectants, textile and food industry, it is widely used in the medicinal industry too. Highly used in preparation of lotions and dressings used in burns and open wounds (N. Savithramma et al., 2011). Plant essence is majorly involved in synthesis of nano sized metal and their oxides. Leaves are awfully involved due to presence of essential phytochemicals including flavonoids, aldehydes, terpenoids etc which are responsible for formulating metal and metal oxide moreover, enhances bio functionality and affinity of these particles (Jaison Jeevanandam et al., 2016). It is reported that nanoparticles show a decline phase in growth of bacteria but use of silver nanoparticles with high doses in stock solution can inhibit growth, even no growth too (shamila shehzadi et al., 2018).

It is revealed by (Yuet Ying Loo et al., 2018) that antibacterial activity against gram negative bacteria (E. coli, K. pneumoniae) which are involved in foodborne illness is confirmed using AgNPs, as clear zones around them showing ability to withstand growth of bacteria. Literature confirms that other bacterial strains including (MRSA) can be hindered using silver nanoparticles. AgNPs can be 32folds stronger against MRSA by setting up a cell wall of bacteria (Faizan Abul Qais et al., 2019). Multidrug resistant Pseudomonas Aeruginosa is shattered effectively by AgNPs. They not only alter the shape and structure of P. aeruginosa but also destroy challenges caused by metabolic and environmental stresses. Superoxide leads to alteration in enzyme activity as well as induce apoptosis effects (Shijing Liao et al., 2019). It is reported that nanoparticles show a decline phase in growth of bacteria but use of silver nanoparticles with high doses in stock solution can inhibit growth, even no growth too (Shamila Shehzadi et al., 2018).

1.2 Antibacterial activity of copper nanoparticles

Historically, it is known that copper is an essential metal after the Stone age and even now, alloy of copper called bronze is used extensively. Today, copper is exercised for making electrical equipment, as heat exchangers and widely used in construction (Richard A.Festa, Dennis J.Thiele, 2011). Copper is known to be more appreciative in nanotechnology due to extraordinary properties, which are enhanced at size on nano-scale. One sensational property of copper nanoparticles is that they enhance the penetrating ability (surface area and pore volume) so that scattered silver nanoparticles are approachable to bacteria (Dagmar Chudobova et al., 2015). Moreover, it is reported that copper nanoparticles show feeble performance against bacterial and other microbial strains as compared to other metallic nanoparticles and oxides of them (Dagmar Chudobova et al., 2015). Oxides of copper I.e. cupric oxide and super oxides of copper responsible for metal ion toxicity in cells of bacterial strains and ultimately leads to death of microbes (Surapaneni Meghana et al., 2015). It turned up that even the medium dosage of copper oxide within stock solution can lead to maximum toxicity in cells which can set a pathway for death (Shamila Shehzadi et al., 2018).

It is clearly mentioned by (Mohammed Ishaque Nabila et al., 2018) eco friendly and much cheaper production of CuO NPs can play a damaging role in inhibition of human pathogenic bacteria. In addition, E coli, P. aeruginosa, staphylococcus aureus and other strains can be killed successfully using copper oxides nanoparticles (Ahamed et al., 2014). It is put up by (Raheem et al., 2019) that CuO nanoparticles are effective proxy against anti-MRSA. It is clear that the zone of inhibition is proportional to concentration of nanoparticles proving to be the best alternative agent to antibiotics against MRSA.

1.3 Antibacterial activity of zinc nanoparticles

Zinc is of extremely commercial importance. It is not only essential to life but also widely used metal. Zinc itself and alloys of zinc are used in prevention of corrosion and rusting. In terms of biology, it is a trace element found in our human body with highest concentration in blood cells and found in pancreas to aid in storage of insulin (Adam Augustyn et al., march 2020). Biologically, oxides of zinc nanoparticles have more impactful role due its marvellous properties of being less toxic, cheap and biostability. ZnO NPs have optimistic effects in the field of Biomedics such as showing anticancer and antibacterial activities moreover it is reported to show effects of antidiabetic treatments. Excellent ZnO NPs also show fluorescence possibility of bioimaging of cellular and subcellular

structures (Jinhuan Jiang et al., 2018). Hence, it is set out that ZnO NPs show remarkable antibacterial abilities by disrupting the cell membrane, DNA, protein content and reducing working ability of human cells (Vishvanath Tiwari et al., 2018).

Several studies have divulged that ZnO NPs interact with various bacterial pathogens contributing to the severe infections to assassinate them. The US FDA has proved that ZnO NPs are regarded as safe against foodborne pathogens. Different concentrations of nanoparticles were tested which disclosed that disorder in cell membrane is the leading cause of death of strains including S. aureus, P. aeruginosa and E. coli (Sirelkhatim et al., 2015). It was repeatedly reported that ZnO NPs are responsible in production of ROS (reactive oxygen species) but along with ROS, generation of hydrogen peroxides which lead to toxicity in cell membrane causing destruction of a bacterial strain. Hence, these particles prove to be the best in inhibiting growth. This is how they attack MRSA and other resistant strains to kill them (Kadiyala et al., 2018).

2. Medicinal plants and it's Antibacterial Potential

According to the World Health Organization (WHO), medicinal plants are best in terms of utilizing and synthesizing drugs. It is investigated that 80% of developed countries use conventional medicines prepared from plants due to their best properties, their well-being and cost effective (Nascimento et al., 2000). Some countries not only synthesize medicinal plants for food, preservatives, appetizers, aromatic scents production but also use them as drugs to cure health issues I.e. bacterial, fungal infections. Moreover, they are required for feed for livestock and biofuel productions (Javed et al., 2013). Most of the food poisoning diseases and illness, is reported to be caused by different bacterial strains. Preventive measures from them are achieved by many chemical agents and chemicals but the drawback is it leaves harmful effects on the human body. Efforts are made to prevent illness against these fatal diseases and keeping food more safe and nutritious, easily degradable and less harmful to human health (A.Mostafa et al., 2018).

2.1 Antibacterial activity of ginger (Zingiber Officinale)

Ginger belongs to the Zingiberace family. It is a rhizome part of a plant. Commonly farmed in countries like Japan, China and India, Nigeria, Indonesia and Jamaica Islands and in Pakistan commercial production is not enough due to restricted cultivation in some districts of Sindh. Ginger is widely used as a seasoning agent in food as well as in many lucrative, such as cookies, candies, teas, jams, syrups in addition, it is regarded as a preservative agent too (Riaz et al., 2015). Treatment of cold illness such as asthma, nausea, shivering and cough etc., loss of craving of the food and problems related to arthritis can be effectively treated by using fresh ginger. Juice and paste of talc ginger are fruitful for relieving headaches around temples and mixed with honey is helpful in weight loss (Ponmurugan Karuppiah and Shyamkumar Rajaram, 2012).

Antibacterial activity of ginger is reported frequently by researchers but crude of ginger, ethanolic powdered form of ginger and boiling of ginger extract show different results against same pathogenic bacteria (Kamrul Islam et al., 2014) reported the result that antibacterial activity of ginger upon boiling drops its antibacterial activity. Crude extracts of ginger and ethanolic powdered form of ginger show good results against foodborne pathogens (Klebsiella pneumoniae, Escherichia coli, Staphylococcus aureus and Pseudomonas aeruginosa) while show excellent result when combined with other factors I.e. garlic, soybean etc. Another study designed to evaluate antibacterial activity of ginger against MRSA and P. aeruginosa declared that it shows, highest inhibition zone against P. aeruginosa than MRSA but better results with MRSA than other resistant strains. It is recommended that active ingredients of ginger should be used to formulate medicines I.e antibiotics in microbiology and pharmacology sectors (Mozhgan Azadpour et al., 2016).

2.2 Antibacterial activity of Garlic cloves (Syzygium Aromaticum)

Garlic cloves (Syzygium Aromaticum) is from the Amaryllidaceae family. Single clove is also known as pearl or solo garlic. It is also said to be a flower bud. It is Asian, Chinese and Italian herb due to being anti-inflammatory, anti-oxidant, anti-bacterial and anti-mutagenic and anti-fungal abilities. Its essential oil is extracted and commonly used for acne, scars and most importantly effective mosquito repellent. Healing, pain relieving capability of clove make it more formidable to use in domestic treatments (Sabahat Saeed and Perween Tariq, 2008). Its natural crude extract, powdered form, fresh slices and paste are all over commercially available and used as preservatives for food. Garlic cloves have a rich history, in terms of its use and benefits. It is declared by literature that garlic was and is regarded as a medicinal plant by Ancient Egyptians. Furthermore, Greece Olympians fed on this aromatic herb to increase their stamina. Hence, it provides users with a bundle of benefits together with seasoning purposes (Kshirsagar et al., 2018).

Staphylococcus aureus, Pseudomonas aeruginosa and Escherichia coli were successfully inhibited by ginger crude extracts and ethanolic

powdered solutions. It is evidently manifested that natural products show excellent results with minimum side effects against pathogenic bacterial strains, this is why it is seen that garlic is common ingredient in organic mouthwashes preventing from bad smell, tooth decay and discoloration (B C Nzeako et al., 2006). Ethanolic extracts and water solution extracts of crude garlic cloves and powdered mixtures with different concentrations showed excellent results against MRSA. This could be the best agent to be used against antibiotics of third generation (Shayamapda Manda et al., 2011).

2.3 Antibacterial activity of Cumin (Cumin Cyminum)

Cumin (Cumin Cyminum) is part of the Apiaceae family. It is regarded as a seed part with a lot important and health benefits. Its antibacterial activity is reported against both gram positive and gram-negative bacterial strains with different concentrations. It is reported, to damage cell membrane and release much of nucleotides and protein content to outside environment. Potential cause on E. coli and P. aeruginosa is reported by (Dua et al., 2013). Commonly used cumin in South East Asia, Central Asia and nearby countries has a lot of latent benefits including physiological processes in the human body leading to antioxidant abilities which helps in scavenging reactive species accompanied in prevention of aging (Ani et al., 2006). Cumin acts as stimulant, carminative, recognized as food preservative against microbial death as well as it imparts characteristic flavor, taste and color to food such as prickles, rice, and mix spices.

To boot, antibacterial activity of cumin with ethanolic, methanolic and aqueous extracts of cumin against S. aureus, E. coli and P. aeruginosa bacterial strains showed fruitful results. Alcoholic extracts showed excellent results compared to aqueous extracts (Al-Shawi et al., 2017). Seeds of cumin are made into refined powdered form and extracts. More is the concentration of cumin less will be bacterial colony of MRSA is observed. This destruction is related wholly to the cell wall. Optimal dosage can lead to antimicrobial and antibacterial effects to combat antimicrobial resistance (Shayamapda Mandal et al., 2011). According to (Perween Tariq et al., 2008), antibacterial activity of cumin aqueous decoctions show good results against P. aeruginosa.

3. Antibiotics and its antibacterial potential

Dynasty of antibiotics has good antibacterial activity, best dispersal throughout the whole body, less toxicity factor, great effectiveness against allowing infection by some bacteria.With excessive use, in fact abuse of antibiotics, bacterial strains develop resistance against them. This resistance against their bacterial activity can be innate or gained. Natural or innate resistance to antibiotics can be caused by species or can be due to absence of a target site. Gained or acquired resistance can be due to mutations or resistance plasmid R. Such resistance can be against antibiotics or its closer family drug only. Basically, antibiotics are ranged according to the formation and anatomy of bacterial strain. Antibiotics target cell wall, disruption leads to lysis of bacteria. They have improved infection causing action moreover, excessive use of antibiotics has made them more resistant. Antibiotics were made to control and prevent infections while excessive use of them have made bacteria to become much stronger than previously by gaining resistance against them (Kapoor et al., 2017). Beta lactam antibiotics are accused of crossing cell walls and causing alterations in porin proteins (pore causing cell diffusion mechanism). Gram positive bacterial strains having high level of peptidoglycan makes it more prone to penicillin family of antibiotics while the gram-negative bacterial strains contain thin layered peptidoglycan with lipopolysaccharides preventing entry of antibiotic into host cell (Chow, Susan., 2018).

3.1 Antibacterial activity of Penicillin

This was the first known antibiotic discovered by Alexander Fleming in 1928. Main target is to burst the cell wall of bacteria which provides structural and mechanical strength to the bacterial cell. It is effective against gram positive or bacterial strains with cell wall making holes in the cell wall while for gram negative bacteria (without cell wall) are effective due to peptidoglycan thin layer (Tim Newman., 2018). Bacteria have become highly adaptive to environment and as a result microbial evolution occur due to genetic variability such as capability of resistance against antibiotics by producing penicillinase to degrade penicillin and create alterations in bacterial structure for its survival (A Brief Overview of Classes of Antibiotics, September 8, 2014). Different antibiotics are tested against bacterial strain MRSA. All the antibiotics show good results with approximately 17-20nm inhibitory zone but with penicillin, it shows satisfactory results by showing 12-16nm inhibition zone, which proves that MRSA has developed a great mechanism of resistance against it. However, synergetic effects of penicillin with other antibiotics, medicinal plants, nanoparticles and along with their derivatives show much better results (Uzair et al., 2017).

3.2 Antibacterial activity of Cephalosporins

First generation of cephalosporins was merely for gram positive bacteria causing holes in the cell wall as mode of action was the same as that of penicillin.

Second generation cephalosporins were potent for gram negative and feeble against gram positive. Third generation cephalosporin is used for both gram positive and gram-negative bacteria such as E. coli, H. influenzae, P. pneumonia (Arumugham et al., 2020). Due to gaining resistance against antibiotics, bacteria have become more powerful that is why generation first to fifth has arrived. Highest resistant strain, Methicillin Resistant Staphylococcus Aureus (MRSA) is inhibited by a novel fifth generation to be arrived at.

3.3. Antibacterial activity of Aztreonam

It is basically selective against gram negative bacteria but indolent against gram positive bacteria. Heavily functional against pseudomonas aeruginosa and its efficacy is the same as gentamicin. Furthermore, union of aztreonam with other antibiotics can be worthwhile against gram positive bacteria too. This class of antibiotics need to be used with great care as they cannot work with good efficacy with penicillin class hence, cross reactivity of this antibiotic is not effective unlike other beta lactam antibiotics (Kishiyama JL et al., 1994).

4. Progressive development against antibacterial activity

Speedy emergence of bacterial resistance against antibiotics across the World has threatened the potency of antibiotics. This is due to excessive public demand, abuse and misuse of antibacterial medications. Now, the call for time is that new advancement should be made in order to cope up with pathogenic bacterial strains. Once bacteria develop resistance against any antibiotic, it transfers into its generations. Resistance can be developed by evolution, by mutations and later it can be transferred through horizontal gene transfer I.e. parents to offsprings. Moreover, low cost of antibiotics has gained public interest and new antibiotics are expensive due to which lavish use has developed a great mechanism within the bacterial community to fight against antibiotics leading to developing resistance (Ventola C. L., 2015). A new approach was to introduce multidrug resistant antibiotics but another biggest problem is the unsure evolution of bacteria. Even if any manufacturer invests money in producing any new product in competition with antibiotics, it will be expensive in the first place. On the other hand, growth of bacteria with new traits is unreliable (Ian M. Gould & Abhijit M. Bal, 2013).

4.1 Nanoparticles with novel strategies against bacterial activity

- Nanoparticles on exposing with bacterial cell walls can upregulate the genes and downregulated genes too which can ultimately disturb protein structures, cell cycles, cellular transports, respiration, biofilm production, central metabolism and most importantly transcription (Slavin et al., 2017).
- Nanotechnology can be fruitful as they in specific form (quantum dots) become active in cells, react with oxygen and other molecules become reactive species helpful killing bacteria and cancer cells by damaging DNA, protein and cellular membranes (Melissae Fellet,2017).
- Most resistant bacteria such as MDROs (multidrug resistant organisms) can be treated with amalgam of antibiotic and nanoparticles. It is reported that using lower concentration of antibiotic augmented with nanoparticles have shown best results as before by targeting the infected site and due to minimum dosage, no toxicity effects occur (Nan-Yao Lee, 2019). Bactericidal activity is observed at 12.5 µg/ml is 100%. 6.25 µg/ml showed 95% killing of cells and 55% death rate of bacteria was observed at 0.78 µg/ml of mixing of antibiotic and nanoparticles by agar diffusion method. This method of gaining capability against bacterial activity will prove effective (Pedro V. Baptista, 2018).

4.2 Gene modulation against bacterial activity

Gene expression of bacteria compels it to create resistance against antibiotics. This resistance is developed and efficacy of antibiotics decreases. Modulation of gene expression which causes resistance can be helpful to reverse the action by altered or silencing of genes (Wang et al., 2017). Activation of resistance gene is done by promoters alterations which could be hybrid promoters or complete promoters. This hybridization is mainly in terms of genes with insertional sequences that are introduced and reinforce promoters to work effectively. Insertion sequences (short sequences that are part of transposable elements present in the genome of a single cell) are mainly responsible for resistance causing genes to function. Modulation of genes expression can be induced by disruption of insertional sequences of genes as reported by literature of (Depardieuet al., 2017).

Conclusion

To conclude, antibiotics usage starting from penicillin has travelled a long way and reached up to fourth and even fifth stage antibiotics to be used nowadays. Pre antibiotic era includes use of herbs and plant extracts as antibacterial agents. Modern era of antibiotics includes broad spectrum antibiotics with minimum side effects which lead to misuse of it. Excessive and extensive use of antibiotics leads to resistance development in bacterial microbes.

Observations reported that bacterial strains can gain resistance by enzymatic degradation and other solid mechanisms against antibiotics and later passing this resistance mechanism to their progeny (Neelam Taneja et al., 2019). This is an alarming situation because not only human medicines have become complicated but also bacterial microbes have developed smarter and clever ways to escape from antibiotics. It was thought that humans will lose race to bacterial infections but scientists kept on working in their domains for developing better strategies to rout out bacteria.

For this, the agriculture department in close relation with biotechnology has developed a defined and vast research on natural immunity booster plants and herbs and spices. Moreover, research on plants with antimicrobial, antibacterial potentials are under constant development to produce natural extracts for curing against bacterial strains. Furthermore, these plant extracts could be more beneficial than antibiotics because they are natural extracts as well as side effects of plant extracts are minimum (Chakraborty et al., 2020). They are easily available and can be grown by giving suitable physical environments. Medicinal plants used in the whole world share ratio of 25%. According to WHO, 252 are the active compounds obtained from medicinal plants and currently 122 are in use which clearly defines that many medicinal plants can show drastic and revolutionized effects against bacterial activities, they remain in research studies (Y.-Z. Shu, 1998). Modern techniques use nanotechnology to develop nanoparticles mainly metallic nanoparticles which are synthesis from natural herbs can be very effective against bacterial strains that have developed resistance against multidrug too. Metallic nanoparticles, oxides and ionic nanoparticles are highly functional to treat bacterial microbes (Hemeg et al., 2017). New game plan to win from bacteria is the use of antibiotics along with nanoparticles which prove to be potent as well as low dosage can lead to less or no toxicity effects. Mainly new approaches include the use of metagenomics to silence or knock out the genes that cause the resistance. Reversal of resistance causing modulation of genes could be part of war.

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