INTRODUCTION

Micro-organisms have developed resistance against antibiotics with the help of biofilms. Biofilms formed by micro-organisms, covers the microbes which prevent the passage of antibiotics and interferes with the interaction between antibiotics and micro-organisms. Biofilms are formed when micro-organisms get attached to the moist surface. After coming in contact to the moist surface, it produces gel-like, slimy contents which are known as biofilms. Micro-organisms encapsulate themselves in this slimy layer, which is known as biofilm. It is made up of extracellular polymeric matrix, produced by micro-organisms [3]. The lifestyle of micro-organisms changes completely on the formation of biofilm. The physiological changes have been observed in the microbes with the formation of biofilms. Biofilms increase the life span of micro-organisms. It also increases the microbial growth rate. Micro-organisms enter inside the host and combat its innate immune defense system with the help of biofilm [8]. Hence, biofilm increases the persistence period of micro-organisms inside the host. Biofilm has the complex structure which reduces the attacking ability of antibiotics. It protects micro-organisms from the attack of antibiotics as it does not allow antibiotics to reach microbial surface [11]. Experiments have been performed which shows that Staphylococcus aureus has become resistant to methicillin as it is covered by biofilms [1]. Polysaccharides, such as silica acid, help in protecting micro-organisms by inhibiting the attack of neutrophils toward microbes. Thus, pathogens which were once considered as extracellular are converted into intracellular with the help of biofilm. It helps microbes to penetrate inside the host [10] (Figs. 1 and 2).

Therapeutics plants have the rich assets of ingredients which are utilized for the development of drugs. There are 8000 species of plants in India which are designated as medicinal plants. Medicinal plants have proved to be the best for the treatment of disease [2]. During secondary metabolism, medicinal plants secrete active compounds which have been helpful in treating infectious disease. Medicinal plants have been used for the extraction, synthesis, and development of drugs. Extracts of methanol and ethanol from the medicinal plants have been studied and it has proved to be effective in treating biofilm and thus, the pathogens [16].

The objective of most of the conventional treatment is to kill or repress the growth of micro-organisms. Continuous exposures to these treatments make micro-organisms resistant toward them. This method affects pathogenic microbes only for a limited period. It has been observed that many pathogenic micro-organisms start developing resistant against such treatment after a certain period [9]. It is because of the virulent factor that they produce during the treatment which makes them resistant. One such virulent factor is biofilm. Biofilm helps bacteria in fighting against the antibiotics treatment and immune system response. Thin, slimy layers of microbes that occur in moist environment are considered as biofilms. Biofilms are impermeable in nature which prevents the passage of antibiotics into the microbes. It has become important to develop new methods or medicines to treat micro-organisms that cause infectious disease. Nanotechnology has proved to be a standout among the most dynamic regions of research and development in advanced medical science. Nanoparticle is the most essential part of nanotechnology. It has proved to be effective in treating many diseases [5].

Nanoparticles are made up of both natural and inorganic materials. Nanoparticles made up from these materials have antibiofilm and antibacterial properties. Experiments have been performed and it has been proved that these nanoparticles can be used for the treatment of drugs which can be used for the treatment of biofilms. This proves that nanoparticle has different mechanisms to control biofilm growth and also different strategies to stop microbial growth and kill them. When the biofilms are treated with nanoparticles, it gets destroyed [20].

The interaction between nanoparticle and biofilm are as follows:

- Nanoparticle is transferred to the biofilm surface
- Nanoparticle gets attached to the surface
Nanoparticles penetrate through the biofilm surface toward the microorganisms [18].

In other words, nanoparticles penetrate into biofilm layer, spoil cell physiology, denature protein, stop the activity of enzymes, and prevent the replication of DNA and interaction of ribosomes [17]. Many factors influence the interaction that occurs between biofilm and nanoparticle. They are physiochemical and biological factors of the biofilm matrix, environmental factors such as water and temperature (Fig. 3).

MEDICINAL PLANTS

Panax ginseng

*P. ginseng* is a therapeutic plant. It has a wide range of pharmacological applications. It contains an active ingredient, ginsenosides, which is useful in treating many infectious diseases. It has been used to treat cancer, neurodegenerative disease, diabetes mellitus, and hypertension. It helps in maintaining the homeostasis of immune system and regulates immune system against microbial attack [7]. Ginseng plants show many properties such as antimicrobial, antibacterial and antiviral properties. This plant was used for the synthesis of gold and silver nanoparticles [36]. These nanoparticles were formed by the reduction of auric chloride and silver nitrate, respectively, and they have been studied and found to be resistant toward biofilm produced by microbes. Silver nanoparticles showed inhibition against biofilm produced by *S. aureus* and *Pseudomonas aeruginosa*. Both gold and silver nanoparticles were also found to have anticoagulant properties [22] (Table 1 and Fig. 4).

Dioscorea bulbifera

There are 600 species under genus *Dioscorea*. Among them, *D. bulbifera* is a novel plant due to its species-specific phytochemistry. Tuber extract of the plant is rich in flavonoids and catechin which provides plant antioxidant and antidiabetic properties. Biofilm compounds of this plant show anti-inflammatory, plasmid curing, anticancer, and antidiabetic properties [4]. Aucore Ag shell nanoparticle was synthesized using the tuber extracts from *D. bulbifera*. These nanoparticles showed highest biofilm inhibition. This leads to the death of cells [19] (Table 2 and Fig. 5).

*S. aureus* is a widely recognized infectious disease which causes skin infection, burn wounds and are resistant to antibiotics. Drug resistance is deadly dispute evolving in today’s world. Recently, microbes resistant to antibiotics are controlled by multi-drug treatments.

**Table 1: Classification of Panax ginseng**

| Kingdom    | Plantae |
|------------|---------|
| Order      | Apiales |
| Family     | Araliaceae |
| Genus      | Panax |
| Species    | *Panax ginseng* |

**Table 2: Classification of Dioscorea bulbifera**

| Kingdom    | Plantae |
|------------|---------|
| Order      | Dioscoreales |
| Family     | Dioscoreaceae |
| Genus      | Dioscorea |
| Species    | *Dioscorea bulbifera* |

**Fig. 1:** *Staphylococcus aureus* biofilm on a moist surface. Source: http://science.howstuffworks.com/life/cellular-microscopic/biofilm4.htm

**Fig. 2:** Stages of biofilm development (1) reversible stage (2) attachment stage (3) formation of biofilm (4) biofilms mature (5) detachment stage. Source: http://www.formatex.info/microbiology4/vol1/179-187.pdf

**Fig. 3:** Nanoparticle penetrating through the biofilm layer and migrating toward bacterial surface. Source: http://journal.frontiersin.org/article/10.3389/fmicb.2015.00591/full

**Fig. 4:** Medicinal plant *Panax ginseng*. Source: http://www.herbs.org/greenpapers/ginseng.htm
In vitro extraction of secondary metabolites from *D. binata* is potent antibacterial agent against *S. aureus*. It disrupts the biofilm layer of bacteria. Silver nanoparticle obtained from the extract of *D. binata* is effective in antibiotic activity. They do not have any cytotoxic impacts on human keratinocytes [15] (Table 3 and Fig. 6).

**Plumbago zeylanica**

*P. zeylanica* belongs to genus *Plumbago* exhibits multiple medicinal properties such as anti-inflammatory, wound healing, antidiabetic, memory inducing, blood coagulation, antimalarial, central nervous system, microbiological, anticancer, antiviral, and antioxidant activities [12]. Root extract of *P. zeylanica* contains sugars, flavonoids, and organic acid. Bimetallic, gold and silver nanoparticles were developed using the root extract of the plant. These nanoparticles affect biofilms produced by *S. aureus, Acinetobacter baumannii*, and *Escherichia coli*. They showed antimicrobial and antibiofilm properties against these microbes [13] (Table 4 and Fig. 7).

**Ruta graveolens**

*R. graveolens* comes under the genus *Ruta*. *R. graveolens* contains acridone alkaloids, flavonoids, coumarines, terpenoids, and volatile substances which give the plant antiandrogenic activity, anti-inflammatory and analgesic properties and anticancer activities [6] (Table 5 and Fig. 8). Silver nanoparticles obtained from *R. graveolens* shows color change on phytochemical reaction. It also shows antibacterial and antibiofilm activity against *Candida albicans, S. aureus*, and *P. aeruginosa* [14] (Table 6).

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**Table 3: Classification of Drosera binata**

| Kingdom | Plantae |
|---------|---------|
| Order   | Caryophyllales |
| Family  | Droseraceae |
| Genus   | Drosera |
| Species | Drosera binata |

**Table 4: Classification of Plumbago zeylanica**

| Kingdom | Plantae |
|---------|---------|
| Order   | Caryophyllales |
| Family  | Plumbaginaceae |
| Genus   | Plumbago |
| Species | Plumbago zeylanica |

**Table 5: Classification of Ruta graveolens**

| Kingdom | Plantae |
|---------|---------|
| Order   | Sapindales |
| Family  | Rutaceae |
| Genus   | Ruta |
| Species | Ruta graveolens |

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*Fig. 5: Medicinal plant Dioscorea bulbifera.*
Source: https://keyserver.lucidcentral.org/weeds/data/media/Html/dioscorea_bulbifera_var_bulbifera.htm

*Fig. 6: Medicinal plant Drosera binata.*
Source: http://cpphotofinder.com/drosera-binata-var-dichotoma-2539.html

*Fig. 7: Medicinal plants Plumbago zeylanica.*
Source: http://cysonline.org/article.asp?issn=2229-5186;year=2012;volume=3;issue=3;spage=178;epage=198;aulast=Kishore

*Fig. 8: Medicinal plant Ruta graveolens.*
Source: http://www.motherearthliving.com/in-the-garden/ruta-graveolens-growing-common-rue
Table 6: Activities of medicinal plants in form of nanoparticles

| Medicinal plants               | Parts used   | Nanoparticles                              | Activity                          | References         |
|-------------------------------|--------------|--------------------------------------------|-----------------------------------|--------------------|
| Pelargonium endlicherianum    | Root extract | Silver nanoparticle                        | Antimicrobial activity            | [46]               |
| Fenzl.                        |              |                                            |                                   |                    |
| Millettia pinnata             | Flower extract | Silver nanoparticle                        | Anticholinesterase, antibacterial, and cytotoxic activities | [47]               |
| Bauhinia acuminata and        | Plant extract | Silver nanoparticle                        | Antimicrobial activity            | [48]               |
| Biophytum sensitivum          |              |                                            |                                   |                    |
| Taraxacum laevigatum          | Plant extract | Platinum nanoparticle                      | Antibacterial activity            | [49]               |
| Pongamia pinnata              | Seeds extract | Silver nanoparticle                        | Antibacterial activity            | [50]               |
| Cassia fistula (Linn,)         | Leaf extract  | Silver nanoparticle                        | Antimicrobial agents; antioxidants | [42]               |
| Panax ginseng                 | Leaf extract, root extract                     | Silver nanoparticle, gold             | Anticancer activity, antimicrobial, antibacterial and antifungal properties, anticoagulant properties, and antibiofilm activity | [22,7,41] |
| Carum copticum                | Root extract | MnFeO nanoparticles coated with PEGylated chitosan | Antibacterial activity | [39]               |
| Ginkgo biloba                 | Leaf extract | Silver nanoparticles                        | Antimicrobial activity            | [37]               |
| Garcinia mangostana           | Rind extract | Gold nanoparticles                          | Antimicrobial activity            | [38]               |
| Cacao                         | Leaf extract | Silver nanoparticles                        | Antibacterial activity and cytotoxicity | [35]               |
| Prunella vulgaris L            | Callus culture | Silver and gold nanoparticles              | Antioxidant                      | [33]               |
| Cassytha filiformis           | Plant extract | Silver nanoparticles                        | Anticancer, antifungal, antimicrobial activity | [34]               |
| Trigonella foenum-graecum     | Seed extract | Lanthanum nanoparticles                    | Antibacterial activity            | [40]               |
| Artocarpus lacucha            | Plant extract | Alginate-chitosan                          | Antibacterial activity            | [32]               |
| Sueaed maritima (L) Dumort     | Plant extract | Silver and gold nanoparticles               | Anti-leukemic activity            | [31]               |
| Linum ustvatisissimum         | Plant extract | ZnO/Zn(0H)2 nanoparticles                 | Antibacterial, antifungal, and antimicrobial activities | [43]               |
| Carissa edulis                | Plant extract | Zinc oxide nanoparticles                    | Antibacterial and antioxidant activities | [27]               |
| Jacaranda minisimofolia       | Flowers extract | Zinc oxide nanoparticles                    | Antimicrobial activity            | [26]               |
| Hydrocotyle rotundofolia      | Leaf extract | Silver nanoparticles                        | Antimicrobial activity            | [29]               |
| Rhus chinensis                | Galls extract | Silver nanoparticles                        | Antimicrobial activity            | [30]               |
| Dioscorea morbifera           | Leaf extract | Silver and gold nanoparticles               | Anticancer activity               | [26]               |
| Isatis tinctoria              | Plant extract | Silver nanoparticles                        | Antileishmanial activity          | [25]               |
| Nopatapotes foetida           | Leaf extract  | Silver nanoparticles                        | Antimicrobial activity            | [23]               |
| Hovenia dalsis                | Plant extract | Silver nanoparticles                        | Anticancer activity               | [24]               |
| Syzygium cumini               | Plant extract | Silver, gold, and bimetallic nanoparticles | Antitubercular agents, antymycobacterial agent | [21]               |

CONCLUSION
Biofilms produced by micro-organisms are accountable for the spread of infectious disease. Biofilms have high resistance against the antibiotics which has become a threat to the human beings. It is because the biofilm restrict the penetration of antibiotics and thus prevents the killing of micro-organisms. Nanoparticles made up of medicinal plants have been observed to be helpful in killing micro-organisms. It has proved to be very significant in treating infectious disease. They have the high penetrating power which helps them to penetrate into the biofilm layer and attack microbial surface. It has been observed that a nanoparticle does not affect any organs when treated to eliminate infectious disease. Nanoparticle increases the efficiency of antibiotics and it not only has antibiofilm activity but also antibacterial, antimicrobial, anticancer, and antioxidant activities.

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