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Ethanobotany based nanostructures used in dentistry

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ABSTRACT

Various modalities of treatment are available for different dental diseases, but the major drawback of these conventional drug therapies is the numerous side effects associated with them. This has led to renewed interest in the discovery of novel anti-infective natural compounds derived from plants. Plants have been the major source of medicine since the time immemorial. The field of nanotechnology has got remarkable potential that can bring considerable improvements to the human health, enhanced use of natural resources, and reduced environmental pollution. Since 1990s, nanotechnology has been exploited for potential medical and dental applications. Nanotechnology in combination with ethanobotany holds promise for advanced plant based diagnostics, targeted drug delivery and biosensors. Dentistry is undergoing yet another change to benefit mankind, by transforming itself to the ethanobotany Nano dentistry. A variety of nanostructures such as Nano robots, Nano spheres, Nano fibers, Nano rods, etc., have been studied for various applications in dentistry. Preventive dentistry has also utilized Nano dentistry and nanoparticle to develop the nanomaterials from plant extracts for inclusion in a variety of oral health-care products. The present paper focuses on the current status and the future implications of nanotechnology in ethanobotany dentistry.

Keywords: *dentistry, ethanobotany, nano dentistry.*

1. INTRODUCTION

1.1. Background.

Herbal drugs and their therapeutic use in oral cavity diseases has been known and successfully used for a long time. Oral cavity lesions are mostly gingivitis and mucositis as well as periodontal diseases. Herbal compounds are recommended in the treatment of serous and purulent gingivitis and mucositis, superficial periodontitis, catarrhal tongue inflammation, toxic oral cavity inflammation and difficult healing of post-operative wounds. Herbal based medicines are administered to sooth oral symptoms of systemic diseases. Plant compound can be a powerful and the dominant drug when an inflammation caused by local irritating factor appears. Most important features of herbal medicament are its anti-inflammatory, antiseptic, analgesic, astringent, edema reducing, soothing and healing accelerating properties [1].

Oral cavity, like other parts of human body, contains natural bacterial flora. The bacteria population changes in time and varies among different people, especially as far as subspecies and species proportions are concerned. However, the general contents of the flora remain constant. Biologic equilibrium of the oral cavity gets broken more often when compared to other parts of the body, and it results in a disease. The reasons may be endogenous (when the immunity gets weaker), when there is an unexpected emergence of bacteria in their non-habitual regions (e.g. after tooth extraction or other injuries) or exogenous (after administration of antibiotics).

1.2. Herbal Medicine.

Knowledge and use of plants as herbal medicines has been in practice in various populations throughout human evolution, beginning when man was learning to select plants for food, and to relieve ailments and diseases [2]. However, during the second half of the twentieth century, especially in the Western world, herbal medicines were gradually replaced by allopathic medicines. Allopathic treatments are currently more widely used than traditional medicines, especially in developed countries. However, most developing countries continue to use these natural medicines, most likely because synthtic drugs are expensive [3]. According to the World Health Organization, 80% of people in developing countries depend on traditional medicinal practices to meet and/or supplement their basic health needs [4].

Currently, despite marketing and encouragement from the pharmaceutical industry during the development of allopathic medicines, a large segment of the population in many countries continues to utilize complementary practices for their health care. Many of these practices are derived from medicinal plants. However, due to economic, political, and social changes that have occurred worldwide, the therapeutic use of these natural resources, which are mainly used by people who cannot afford different treatments, has greatly diminished [2, 5]

Elucidating the chemical composition of medicinal plants and their popular uses has become a research focus for all scientific communities. This research may lead to increasingly innovative products, with fewer side effects than existing drugs [6]. Furthermore, the enormous diversity of structures of natural products, as well as their physicochemical and biological properties, has impressed researchers. However, except when they are used for local health care needs, a low percentage of plants have been tested for their medicinal potential. Therefore, there is a lack of information to describe any true potential [7, 8, 9]. The biological activity of medicinal plants from all over the world has

been studied by several groups of researchers. These studies are based on the popular uses of different species, as well as on popular knowledge and scientific studies describing medical plant use, with a focus on how these plants could benefit the pharmaceutical industry [10]. Approximately 50% of the drugs approved during 1981–2006 were directly or indirectly derived from natural products. The chemical complexity of extracts is an extremely important consideration for the success of a formulation, because the formulation must also release the active pharmaceutical ingredient. Consequently, vehicles must concurrently improve the solubility of the drug, minimize the degradation process, reduce any toxicity, and mask any bad taste, while controlling the active absorption and biological response [11, 12]. Phytochemical and phytopharmacological sciences have already established the composition and biological activities of several medicinal plant products. Most of the biologically active constituents of extracts, such as flavonoids, tannins, and terpenoids, are highly water-soluble, but demonstrate a low absorptiondue to their inability to cross lipid membranes, high molecular sizes resulting in loss of bioavailability and efficacy. Some studies have shown that herbal medicines have good activity in assays *in vitro*, which are not reproducible in experiments *in vivo*. Furthermore, some essential substances are rarely used, because they are incompatible with other components in the formulation, or have undesirable properties [13, 14].

1.3. The use of medicinal plants in dental treatment.

There are many factors predisposing oral cavity inflammations. They can be physiologic (age, pregnancy, malnutrition, xerostomia), general (hormonal disturbances, systemic diseases, the use of antibiotics) or local (injuries or operations in the oral cavity area). Under such circumstances a harmless bacteria existing in the oral cavity may become a pathogen, which adheres to the mucosa and cannot be removed by saliva flow. It breaks the protective influence of physiological flora, host's immune system and finally penetrates the tissue. The virulence of micro -organisms is their relative capability to cause disease, which is due to intrinsic characteristics of the bacteria called virulence factors [16]. Pathological lesions of the oral mucosa are a common problem in dental practice. However, peculiar environment of oral cavity, resulting in minimized effect of the medication, structure and physiology of the mucosa, influence of the physiological flora, and the role of saliva and food, temperature and pH changes are important factors restricting the use of the drug. Medicines including herbal compounds are quite often used in dental treatment. Some of them can inhibit bacterial growth; they also have antibacterial, antimycosal and antiviral properties. Herbal drugs of proper concentration of chemically active substances do not irritate or interrupt natural flora. Due to their antibacterial and anti-inflammatory properties, herbal drugs are often added to tooth pastes, where they inhibit growth of tooth plague and bacterial adherence to the pellicle. Rinse solutions, aerosols, unguents and gels, containing anti-inflammatory and antibacterial plant substances are widely used in dental treatment [17]. They are used locally on affected mucosa. The plant-based medicaments can be either infusions or decoctions, prepared from herbal raw materials, or ready-made tinctures or ethanolic and aqueous extracts. Laboratory and clinical examination showed that tooth pastes containing herbal extracts reduce dental plague and gingivitis, tooth staining and dental calculus. Herbal tooth pastes have antibacterial properties; they inhibit the growth of bacteria such as *Streptococcus sobrinus* and *Streptococcus mutans*. It has also been proved that herbal pastes have longer local capacity compared to pastes not containing natural substances [18].

Oral hygiene solutions, containing natural herbal substances, inhibit forming of tooth plaque, change pH by alkalizing the saliva and reduce gingival bleeding. Herbal mixtures can be used additionally to daily hygiene and in periodontal treatment as well. Miswaki sticks used for cleansing teeth and chewing in the Third World countries are in fact a natural toothbrush. Such method of daily oral hygiene is the only oral hygienic procedure in many regions. It has been noticed that the plants miswaki contain antibacterial compounds, which prevent caries and gingivitis [19]. It has been proved that some herbs inhibit keratosis and progress of leukoplakia. The use of herbal extracts has also positive effect on treatment of oral lichen planus lesions. Herbs owe their healing properties to biologically active compounds they contain. Some of these compounds were isolated or obtained by bio-guided isolation after previously detected characteristic activity of the part of the plant. These compounds are flavonoids, coumarins, iridoid glycosides, phenolic acids, resins, triterpens, phytoesters, choline, carotenoids, tannins, vitamins and mineral salts (magnesium, iron, lithium) and essential oils. The most popular are flavonoids and essential oils. Examinations explained that the most probable effect of flavonoids which seem to be natural antibiotics are also effective against oncogenic viruses and carcinogens. Flavonoids, on entering the cell, block the DNA and RNA polymerase which results in inhibition of synthesis of bacterial nucleic acids. Bacterial cell division is therefore impossible. Flavonoids can be used in the treatment of infections caused by *Staphylococcus aureus* and gastrointestinal infections.

Essential oils show a wide spectrum of biological activities and hence are called "volatile phytoncides". They are a very complex blend of organic compounds. Some of them contain up to 300 ingredients per single oil. Nowadays, approximately 3000 compounds contained of oils are known, mostly isoprenoides, benzene and compounds of sulphur and nitrogen [20].

Essential oils show strong destructive effect on viruses, bacteria, saccharomycetes, moulds and protozoans. Phenols, especially carvacrol, thymol and eugenol are those of the strongest activity [21].

Eugenol is widely used in dental treatment. It is the most important compound of dianthus oil with strong antibacterial and anesthetic properties. Eugenol is added to root canal sealers (Endomethasone, Caryosan), to temporary fillings and to pastes used for direct pulp capping (Caryosan, zinc oxide). Eugenol can be also used in disinfection of the tooth canals in the treatment of pulp necrosis or as a precipitator while impregnating the dentin with silver nitrate [22].

Thymol and carvacrol are components of thyme, origanum and satureja oils. Thymol precipitates in the form of blank crystals of strong thyme smell. It has antibacterial and antimycosal properties. It can be used in 1–10% alcohol solutions to disinfect root canals in the treatment of pulp necrosis. Strong antibacterial and antimycosal activity is also a feature of aliphatic alcohols and

leaf aldehydes, which are synthesized in almost all green plants. They serve as a carrier of green fragrance ("green leaf"). A very important characteristic of some of essential oils is their activity against microorganisms resistant to synthetic antibiotics. It is assumed, that microorganisms are unable to become resistant to essential oils. It has been proved in cases when peppermint, eucalyptus and dianthus oils were used. The use of both antibiotic and essential oil has a synergistic effect. The properties of essentials oils have been known since ancient times. The oils have been used in treatment and in protection against "pestilential air" during epidemics. Nowadays, essential oils are used both in prophylactics and treatment [23].

1.4. Action of purified phytocompounds against oral infections.

The following segment describes the studies of phytochemicals that have been shown to be active against oral microbes. The studies are grouped according to the general classes of phytochemicals investigated. Flavonoids and other polyphenols in a study of a number of methanolic plant extracts, two active, artocarpin and artocarpesin and isoprenylflavones were isolated from *Artocarpus heterophyllus* (Moraceae). These inhibited the growth of numerous cariogenic oral bacteria, including *S.mutans* and other oral bacteria, at MIC values of 3.13–12.5 μg/mL In a study of a number of methanolic plant extracts, two active, artocarpin and artocarpesin and isoprenylflavones were isolated from *Artocarpus heterophyllus* (Moraceae) [24].

Flavonone phytoalexins from *Sophora exigua* (Leguminosae) shows to inhibit the growth of a number of cariogenic bacteria, with 5,7,2_,4_-tetrahydroxy-8-lavandulylflavanone being the most active. *Erythrina variegata* (Leguminosae) is used in traditional medicine in tropical and subtropical regions and shows a number of biological properties, including antibacterial activity. *Morus alba* (Moraceae) has been used as a traditional medicine in Asian countries and exhibits antibacterial activity against food poisoning microbes. The compound displayed an MIC of 8 μg/mL against S. mutans, which was comparable to vancomycin and chlorhexidine (1 μgmL-1). A similar mode of antibacterial activity has been reported for isopanduratin isolated from Kaempferia pandurate (*Zingiberaceae*). Components of tea (Camelia sinensis, Theaceae), exhibit anticariogenic effect through various modes of action, including prevention of adherence of bacteria to tooth surfaces, inhibition of production of glucan, bactericidal effects on oral bacteria and amylases inhibition 24 Monomeric polyphenols, particularly simple catechins such as epicatechin, epicatechin gallate and epigallocatechin gallate are believed to be the culprit for these biological effects [25].

The paste of leaves of *Psidium guajava* (*Myrtaceae*) has been used traditionally to maintain oral hygiene. The anti-adherent properties of this plant were supported by the reduction of cell-surface hydrophobicity observed in early settled‖ plaque bacteria (*S.sanguinis, S.mitis* and *Actinomyces*) exposed to guava extract (1mg/mL). Recently, a proteomics approach a low concentration (1.6%, v/v) of a *Psidium cattleianum* water extract resulted in the down regulation of genes involved in lactic acid production, general metabolism and glycolysis. At higher concentrations (25–100% v/v), the extract inhibited *S. mutans* biofilms. Macelignan (20 μg/mL) displayed pronounced antibacterial activity and eliminated viable *S. mutans* within 1 min. Macelignan also displayed antibiofilm action against *S. mutans, S. sanguis* and A.viscosus. Naringin, a polymethoxylated flavonoid found in citrus fruits and an FDA-approved health supplement, inhibits the growth of periodontal pathogens and other common oral microorganisms (9.8– 125mg/mL) [26].

1.5. Terpenes.

Bakuchiol from Ayurvedic medicinal plant, *Psoralea corylifolia* (Fabaceae), has shown activity against numerous Gram-positive and Gram-negative oral pathogens (MIC = 1–4 μg/mL). It was able to inhibit the growth of *S. mutans* under a range of sucrose concentrations, pH values and in the presence of organic acids in a temperature-dependent manner and also inhibited the growth of cells adhered to a glass surface [27].

1.6. Sugar Alcohols.

Xylitol is a sugar alcohol found in plants used as an artificial sweetener in varieties of foods. It has anticariogenic properties which were investigated by adding 0.78–50% xylitol to broth cultures of *S. mutans, S. sanguis* and *S. salivarius* incubated at 37°C for 18 hrs and optical density of the cultures were determined. *S.mutans* was the only bacterium inhibited by xylitol at 1.56%, while all other bacteria showed statistically significant inhibition at levels above 1.56%. The study revealed that xylitol exhibited anticariogenic effects by inhibiting the growth of *S. mutans* while not affecting other streptococci as part of the normal oral flora [28].

1.7. Other Phytochemicals.

Constituents found in hops (female flower clusters of a species *Humulus lupulus* from Cannabaceae), have been found to display antibacterial action against *S. mutans, S. sanguis* and S. saliviarius in disc diffusion assays. These antibacterial actions intensified in the presence of ascorbic acid, suggesting that this effect was due to the acidic nature of ascorbic acid. The antimicrobial properties of a number of commercially available dentifrices containing natural products have been evaluated against oral microorganisms [29].

2. GENESIS OF NANOTECHNOLOGY

2.1. About Nanotechnology.

The prefix "nano" in the nanotechnology means a billionth (1×10^{-9}). "Nanotechnology" is based on the recognition of the particles less than the size of 100 nanometers (nm) impart to nanostructures built from them new properties and behavior. This happens because particles, which are smaller than the characteristic lengths associated with particular phenomenon often, display new chemistry and physics, leading to new behavior which depends on the size. On the other hand, "nanotechnology" is a process by which the ability to manipulate individual atoms and molecules can be developed using onset of precise tools to build and operate proportionately smaller set. In recent years, nanotechnology has become one of the most important and exciting forefront fields in science. It shows great promise for providing us in the near future with many breakthroughs that will change the direction of technological advances in a wide range of applications.

Research and development of this futuristic field is directed towards creating improved material, devices and systems that exploit the new properties [30, 31].

To emphasize more clearly, "nanotechnology" is the engineering and manufacturing of materials at the atomic and molecular scale. In its strictest definition, "nanotechnology" refers to structures roughly in the 1-100 nm size regimes in at least one dimension. Despite this size restriction, "nanotechnology" commonly refers to structures that are up to several hundred nano meters in size, and that are developed by top-down or bottom-up engineering of individual components. The emergence of nanotechnology platforms can enable development and commercialization of entirely new classes of bioactive macromolecules that need precise intracellular delivery for bioactivity. While both organic and inorganic technologies are under development, controlled-release polymer technologies and liposomes will likely continue to have the greatest clinical impact for the foreseeable future [32]. Hence, the recent focus is on the use of nanotechnology for "phytotherapy" or treatment of various diseases by herbal medicines/drugs, including herbal drug delivery where current and emerging nanotechnologies could enable entirely novel classes of therapeutics. The herbal medicines are not a simple task since many factors influence the biological efficacy and reproducible therapeutic effect. Standardized herbal products of consistent quality and containing well-defined constituents are required for reliable clinical trials and to provide consistent beneficial therapeutic effects. Pharmacological properties of an herbal formulation depend on phytochemial constituents present therein. Development of authentic analytical methods which can reliably profile the phytochemical composition, including quantitative analyses of market/bioactive compounds and other major constituents, is a major challenge to scientists. The nanotechnology based herbal drugs possess improved solubility and enhanced bioavailability [33].

2.2. Approaches in Nanotechnology.

Nanotechnology is an advanced scientific technique in the 21st century. By analyzing the relationship between nanotechnology and biological medicine, the application of nanotechnological methods for bioavailability enhancement of herbal drugs can be brought about. It is indicated that nanotechnology is one of the fastest developmental, the most potential and the far-reaching high and new technology in the present era, and it greatly promotes the development of biological medicine and bioavailability enhancement of herbal drugs. With the application of nanotechnology for nanomization of herbal drugs, it will make the development of nanoherbal drugs possess high bioavailability, which consequently will open the new era of herbal drug discovery [34]. The breakthrough in this regard will be achieved from the research of the nanomization of herbal drugs against cancer and various other diseases. Three approaches have been followed in production of nanoparticles, namely Bottom up approach, Top down approach and functional approach [35]. The functional approach disregards the method of production of a nanoparticle, and the objective is to produce a nanoparticle with a specific functionality. The fields of science and technology have witnessed the fabrication of several nanoparticles that we come across and use in our day to day lives, many a times not realizing it is part of the future revolution. The various nanoparticles are nano pores, nanotubes, quantum dots, nanoshells, dendrimers, liposomes, nanorods, fullerenes, nanospheres, nanowires, nanobelts, nanorings, nanocapsules [36].

Use of nanotechnology in medicine and more specifically drug delivery is set to spread rapidly. Presently, many substances are under investigation for drug delivery and more specifically for cancer therapy. Interestingly, pharmaceutical sciences are using nanoparticles to reduce toxicity and side effects of drugs. From a positive view point, especially the potential to cross the blood brain barrier may open new ways for drug delivery into the brain. In addition, the nanosize also allows for access into the cell and various cellular compartments, including the nucleus. A multitude of substances are currently under investigation for the preparation of nanoparticles for drug delivery, varying from biological substances like albumin, gelatin and phospholipids for liposomes, and more substances of a chemical nature like various polymers and solid metal containing nanoparticles [37].

Herbal drugs have now occupied lead positions in the pharmacopoeia and the improvement in this concern through nanoformulations using nanotechnology have been done. Known effects and no side effects have made natural products/herbal drugs a powerful therapeutic solution to the organisms. But the delivery of plant/herbal therapeutic molecules as drugs is problematic due to poor solubility, poor permeability, low bioavailability, instability in biological milieu and extensive first pass metabolism. These limitations of herbal drugs can be overcome by attaching or encapsulating them with suitable nanomaterials. The nanomaterials can significantly enhance the pharmacokinetics and therapeutic index of plant drugs. Targeted delivery and combination therapy can drastically improve the performance of herbal drugs [38].

2.3. Nanotechnology in the field of medicine.

Advancement in the field of nanotechnology and its applications to the field of medicines and pharmaceuticals has revolutionized the twentieth century. Nanotechnology is the study of extremely small structures [39]. The prefix "nano" is a Greek word which means "dwarf". The word "nano" means very small or miniature size. Nanotechnology is the treatment of individual atoms, molecules, or compounds into structures to produce materials and devices with special properties. Nanotechnology involve work from top down i.e. reducing the size of large structures to smallest structure e.g. photonics applications in nano electronics and nano engineering, top-down or the bottom up, which involves changing individual atoms and molecules into nanostructures and more closely resembles chemistry biology. Nanotechnology deals with materials in the size of 0.1 to 100 nm; however it is also inherent that these materials should display different properties such as electrical conductance chemical reactivity, magnetism, optical effects and physical strength, from bulk materials as a result of their small size. Nanotechnology works on matter at dimensions in the nanometer scale length (1-100 nm), and thus can be used for a broad range of applications and the creation of various types of nano materials and nano devices.

2.4. Nanotechnology in health and medicine.

Even today various disease like diabetes, cancer, Parkinson's disease, Alzheimer's disease, cardiovascular diseases and multiple sclerosis as well as different kinds of serious inflammatory or

infectious diseases (e.g. HIV) constitute a high number of serious and complex illnesses which are posing a major problem for the mankind [40]. Nanomedicine is an application of nanotechnology which works in the field of health and medicine. Nano-medicine makes use of nano materials, and nano electronic biosensors. In the future, nano medicine will benefit molecular nanotechnology. The medical area of nano science application has many projected benefits and is potentially valuable for all human races. With the help of nano medicine early detection and prevention, improved diagnosis, proper treatment and follow-up of diseases is possible. Certain nano scale particles are used as tags and labels for the biological diagnostics can be performed quickly, the testing has become more sensitive and more flexible. Gene sequencing has become more efficient with the invention of nano devices like gold nano particles, these gold particles when tagged with short segments of DNA can be used for detection of genetic sequence in a sample. With the help of nanotechnology, damaged tissue can be reproduced or repaired. These so called artificially stimulated cells are used in tissue engineering, which might revolutionize the transplantation of organs or artificial implants. Advanced biosensors with novel features can be developed with the help of Carbon nano tubes. These biosensors can be used for astrobiology and can throw light on study origins of life. This technology is also being used to develop sensors for cancer diagnostics. Though CNT is inert, it can be functionalized at the tip with a probe molecule. Their study uses AFM as an experimental platform.

i. Probe molecule to serve as signature of leukemia cells identified.

ii. Current flow due to hybridization will be through CNT electrode to an IC chip.

iii. Prototype biosensors catheter development. Nanotechnology has made excellent contribution in the field of stem cell research.

For example, magnetic nanoparticles (MNPs) have been successfully used to isolate and group stem cells. Quantum dots have been used for molecular imaging and tracing of stem cells, for delivery of gene or drugs into stem cells, nano materials such as carbon nano tubes, fluorescent CNTs and fluorescent MNPs have been used. Unique nanostructures were designed for controllable regulation of proliferation and differentiation of stem cells is done by designed unique nano structures. All these advances speed up the development of stem cells toward the application in regenerative medicine [41]. The recent applications of nanotechnology in stem cell research promises to open new avenues in regenerative medicine. Nanotechnology can be a valuable tool to track and image stem cells, to drive their differentiation into specific cell lineage and ultimately to understand their biology. This will hopefully lead to stem cell-based therapeutics for the prevention, diagnosis and treatment of human diseases. Nano devices can be used in stem cell research in tracking and imaging them. It has its applications for basic science as well as translational medicine. Stem cells can be modulated by mixing of nano carriers with biological molecules. Nano devices can be used for intracellular access and also for intelligent delivery and sensing of biomolecules. These technologies have a great impact in stem cell microenvironment and tissue engineering studies and have a great potential for biomedical applications [42]. Medical use of Nano Materials Nano medicine is a relatively new field of science and technology. By interacting with biological molecules at nano scale, nanotechnology broadens the field of research and application. Interactions of nano devices with bio molecules can be understood both in the extracellular medium and inside the human cells. Operation at nano scale allows exploitation of physical properties different from those observed at micro scale such as the volume/surface ratio. Two forms of nano medicine that have already been tested in mice and are awaiting human trials; use of gold nano shells to help diagnose and cure cancer, and the use of liposome as vaccine adjuvants and as vehicles for drug transport [27]. Similarly, drug detoxification is also another application for nano medicine which has been used successfully in rats

Medical technologies can make use of smaller devices are less invasive and can possibly be implanted inside the body, and their biochemical reaction times are much shorter. As compared to typical drug delivery nano devices are faster and more sensitive [43]. Drug Delivery In nanotechnology nano particles are used for site specific drug delivery. In this technique the required drug dose is used and side-effects are lowered significantly as the active agent is deposited in the morbid region only [44]. This highly selective approach can reduce costs and pain to the patients. Thus variety of nano particles such as dendrimers, and nano porous materials find application. Micelles obtained from block co-polymers, are used for drug encapsulation. They transport small drug molecules to the desired location. Similarly, nano electromechanical systems are utilized for the active release of drugs. Iron nano particles or gold shells are finding important application in the cancer treatment. A targeted medicine reduces the drug consumption and treatment expenses, making the treatment of patients cost effective. Nano medicines used for drug delivery are made up of nano scale particles or molecules which can improve drug bioavailability. For maximizing bioavailability both at specific places in the body and over a period of time, molecular targeting is done by nano engineered devices such as nano robots [45]. The molecules are targeted and delivering of drugs is done with cell precision. In vivo imaging is another area where Nano tools and devises are being developed for in vivo imaging. Using nano particle images such as in ultrasound and MRI, nano particles are used as contrast. The nano engineered materials are being developed for effectively treating illnesses and diseases such as cancer. With the advancement of nanotechnology, self-assembled biocompatible nano devices can be created which will detect the cancerous cells and automatically evaluate the disease, will cure and prepare reports. The pharmacological and therapeutic properties of drugs can be improved by proper designing of drug delivery systems, by use of lipid and polymer based nano particles [28]. The strength of drug delivery systems is their ability to alter the pharmacokinetics and biodistribution of the drug. Nano particles are designed to avoid the body's defence mechanism [46] can be used to improve drug delivery. New, complex drug delivery mechanisms are being developed, which can get drugs through cell membranes and into cell cytoplasm, thereby increasing efficiency. Triggered response is one way for drug molecules to be used more efficiently. Drugs that are placed in the body can activate only on receiving a particular signal. A drug with poor solubility will be replaced by a drug delivery system, having improved solubility due to presence of both

hydrophilic and hydrophobic environments [47]. Tissue damage by drug can be prevented with drug delivery, by regulated drug release. With drug delivery systems larger clearance of drug from body can be reduced by altering the pharmacokinetics of the drug. Potential nano drugs will work by very specific and well understood mechanisms; one of the major impacts of nanotechnology and nanoscience will be in leading development of completely new drugs with more useful behavior and less side effects. Thus nano particles are promising tools for the advancement of drug delivery, as diagnostic sensors and bio imaging. The bio-distribution of these nanoparticles is still imperfect due to the complex host's reactions to nano- and micro sized materials and the difficulty in targeting specific organs in the body [48]. Efforts are made to optimize and better understand the potential and limitations of nano particulate systems. In the excretory system study of mice dendrimers are encapsulated for drug delivery of positively-charged gold nano particles, which were found to enter the kidneys while negatively-charged gold nanoparticles remained in the important organs like spleen and liver [44, 49]. The positive surface charge of the nanoparticle decreases the rate of opsonisation of nanoparticles in the liver, thus affecting the excretory pathway. Due to small size of 5 nm, nano particles can get stored in the peripheral tissues, and therefore can get collected in the body over time. Thus nano particles can be used successfully and efficiently for targeting and distribution, further research can be done on nano toxicity so that its medical uses can be increased and improved.

2.5.The clinical application of nanotechnology in operative dentistry.

Nanotechnology aims at the creation and utilization of materials and devices at the atomic, and molecular level, supra molecular structures, and in the exploitation of unique properties of particles of size 0.1 nm to 100 nm. Nano filled composite resin materials are believed to offer excellent wear resistance, strength, and ultimate aesthetics due to their exceptional polishability and luster retention. In operative dentistry, nano fillers constitute spherical silicon dioxide (SiO2) particles with an average size of 5-40 nm [50, 51] . The real innovation about nano fillers is the possibility of improving the load of inorganic phase. The effect of this high filler load is widely recorded in terms of mechanical properties. Micro hybrid composites with additional load of Nano fillers are the best choice in operative dentistry[29]. It is expected that in near future, it would be possible to use a filler material in operative dentistry, whose shape and composition would closely mimic the optical and mechanical characteristics of the natural hard tissues (enamel and dentin). It also explains the basic concepts of fillers in composite resins, scanning electron microscopy and energy dispersive spectroscopy evaluation, and filler weight content. Nanocomposite resins are non-agglomerated discrete nanoparticles that are homogeneously distributed in resins or coatings to produce nanocomposites have been successfully manufactured by nano products Corporation. The nanofiller used are aluminosilicate powder with a mean particle size of 80 ran 1:4 M ratio of alumina to silica and a refractive index of 1.508. These nano composites have superior hardness, flexural strength, modulus of elasticity, decreased polymerization shrinkage and also have excellent handling properties particle size of 80 ran 1:4 M ratio of alumina to silica and a refractive index of 1.508 [52].

2.6. Nanotechnology in oral and maxillofacial surgery.

Local anaesthesia: Most dental procedures involve administration of local anaesthesia and several patients defer their dental treatment for the fear of injections. Truly painless methods of administration of local anaesthesia may be achievable by the application of nanotechnology. Hypothetically, a colloidal suspension containing millions of active analgesic micron-size dental robots will be instilled on the patient's gingiva. After contacting the surface of the crown or mucosa, the ambulating nanorobots would reach the pulp via the gingival sulcus, lamina propria and dentinal tubules guided by chemical gradients and temperature differentials under the control of the dentist with the help of nanocomputer [53]. Once installed in the pulp, these robots may shut down all sensitivity in any particular tooth that requires treatment. After the procedures are completed, these nanorobots may be manipulated to restore all sensation and relinquish control of nerve traffic and egress from the tooth by similar means used for ingress [54].

2.7. Nanotechnology in orthodontic treatment.

Sliding a tooth along an arch wire involves frictional type of force that resists this movement. Use of excessive force might cause root resorption and loss of anchorage. By coating the orthodontic wire with inactive fullerene-like tungsten disulfide nanoparticles known for their excellent dry lubrication properties, a reduction in this friction was observed by Redlich et al.[55]. In future, these nanorobots could directly manipulate periodontal tissues thus allowing a rapid, painless tooth straightening, rotating, vertical repositioning within minutes to hours.

2.8. Nanotechnology in prosthodontics.

Impression materials: Nanofillers are integrated in vinyl poly siloxanes, thus producing unique addition silicone impression materials. This material is claimed to have better properties such as flow, adhesiveness. It also has improved hydrophilic properties hence fewer voids at margin and better model pouring and enhanced detail precision [56].

Implants: The most frequent cause of failure of implants is insufficient bone formation around the biomaterial immediately after implantation, with coating of nanoparticles over the dental implants, adhesion and integration to surrounding tissues is improved [57, 58]. The surface of the implant which may be 'macro', 'micro' or 'Nano' structured plays a main and critical role in determining biocompatibility and bio integration because it is in direct contact with the tissues. The nanostructured materials can exhibit enhanced mechanical, electrical, magnetic, optical properties compared with the conventional micronscale or macro – scale counterparts [59, 60].

Nanotechnology in periodontics Dentinal hypersensitivity: Natural hypersensitive teeth have eight times higher surface density of dentinal tubules and diameter twice as large as non-sensitive teeth. Dental nanorobots could selectively occlude these tubules within minutes and thus offers patients a quick and permanent cure [61, 62]. These nanorobots reach the dentinal tubules and proceeds toward the pulp, guided by chemical gradients, temperature differentials, all under the control of nanocomputer. They can reach the pulp in approximately 100 seconds thereby offering a rapid relief of sensitivity [63]. Drug delivery: Periodontal therapy requires local delivery of drugs for more predictable results of treatment. Drug delivery systems based

on triclosan incorporated nanoparticles have been developed. Pinon-segundo et al. have produced triclosan-loaded nanoparticles by the process of emulsification-diffusion, in an attempt to obtain a novel delivery system for the treatment of periodontal disease . Tetracycline based microspheres are also being evaluated for placement in periodontal pockets. Nanotechnology in conservative dentistry and endodontics Tooth durability and appearance: Durability and appearance of tooth may be improved by replacing enamel layers with covalently bonded artificial materials like diamond and sapphire. They have 20 times more hardness and failure strength than the conventional ones and are also biocompatible. Nanorobotic dentifrice (dentifrobots) delivered by mouth wash or tooth paste could prevent accumulation of supra and subgingival calculus and may also metabolize the trapped organic matter into odorless, harmless vapors and aid in calculus debridement. They measure 1-10 micron and also may have the property to deactivate them if swallowed [64].

2.9. Nanoparticulate based disinfection in endodontics.

The efficacy of nanoparticles to disinfect root canals has gained popularity in the recent past. This has been attributed to the broad spectrum of spectrum antibacterial activity. The nanoparticles evaluated on endodontics include Chitosan, zinc oxide and silver. The efficacy of chitosan and zinc oxide nanoparticles against Enterococcus fecalis has been attributed to their ability to disrupt the cell wall. In addition, these nanoparticles are also able to disintegrate the biofilms within the root canal system [65]. Silver nanoparticles are being evaluated for use as root canal disinfecting agents. It has been shown that 0.02% silver nanoparticle gel is able to kill and disrupt Enterococcus faecalis biofilm [66]. Another revolutionary introduction in the field of endodontics, the fundamental basis of which lies in nanotechnology, is bioactive has been suggested for root canal disinfection.The antimicrobial effect of bioactive glass is due its ability to maintain an alkaline environment over a period of time [67].The efficacy of 45S5 bioactive suspension – nanometric/micrometric hybrid as an antimicrobial agent showed that a ten-fold increase in silica release and 3 units of pH elevation was found with the nanometric bioactive glass [68, 69].

Nanotechnology is foreseen to change health care by serving as a novel method for disease diagnosis and prevention, drug delivery and gene therapy. Although nanotechnology appears to introduce ground breaking techniques and devices in the dental field, there are some concerns as well. These include economical nanorobot mass production technique, ethical issues and human safety, biocompatibility issues and the expertise in precise positioning and technique [70]. Nanotechnology will revolutionize health care, especially dentistry, more profoundly than many other developments of the past. It has the potential to bring out significant benefits, such as improved health. However, as with any other technology, it also carries a potential for misuse and abuse. The evolution of nanotechnology will help dentists with more precision made materials, drugs and equipments by which both the safety and patient compliance are enhanced.

3. NEED OF NANOTECHNOLOGY IN HERBAL MEDICINE

3.1. Prerequisite for herbal medicine to go ahead with nanotechnology.

Since ancient days, natural products, including plants, have been the basis of treatment of human diseases. The basis of concept of modern medicine development remains rooted in traditional medicine and therapies [71, 72]. In different parts of the world like ancient China, Egypt, Africa, America, and India, plants had been used for medicinal purposes long before recorded history. Chemical analysis first became available in the early 19th century which started the extraction and modification of herbal ingredients [71, 73]. For a long time, herbal medicines were not considered for development as novel formulations owing to lack of scientific justification and processing difficulties, such as standardization, extraction, and identification of individual drug components in complex polyherbal systems. However, modern phytopharmaceuticals research solves the scientific needs for herbal medicines as in modern medicine, which gives way for developing novel formulations such as nanoparticles, microemulsions, matrix systems, solid dispersions, liposomes, SLNs, and so on. Nanomicellar system, [74] nanotubes, [75] and colloidal nanogels have been developed for curcumin to be used alone as well as in combination with other chemotherapeutic agents like paclitaxel [34].

Before reaching to the blood, many constituents of the herbal drugs will be smashed in the highly acidic pH of the stomach and other constituents might be metabolized by the liver. Resultant, the optimum quantity of the herbal drugs may not reach the blood. If the drug does not reach in the optimum amount to the infected region at "minimum effective level," then there will be no means to show the therapeutic effect of the drug. Nanocarriers applying to herbal remedies will carry optimum amount of the drug to their site of action bypassing all the barriers such as acidic pH of stomach, liver metabolism and increase the prolonged circulation of the drug into the blood due to their small size [34, 76].

Herbal remedies were selected as feasible drug candidate for delivery through a nano delivery system because of the following properties:

- Effective chloroform, petrol, acetone, and methanolic extracts are available which may not be suitable for delivery as such.
- These are the bulk drugs so dose reduction is intended.
- Currently marketed formulations lack target specificity for various chronic diseases.
- Some other side effects are associated with currently marketed formulations.
- Patient non-compliance due to large doses and less effectiveness with the available formulations.

3.2. Drawbacks of Traditional drug delivery system.

Nano-sized delivery system was selected because of the following reasons:

- They appear to be able to deliver high concentrations of drugs to disease sites because of their unique size and high loading capacities [34].
- Deliver the drug in the small particle size that enhances the entire surface area of the drugs allocating quicker dissolution in the blood.

- The concentration seems to persist at the sites for the longer periods [34].
- Shows EPR (enhanced permeation and retention) effect, i.e., enhanced permeation through the barriers because of the small size and retention due to poor lymphatic drainage such in tumor [34].
- Exhibits passive targeting to the disease site of action without the addition of any particular ligand moiety [34].
- Decrease in the side effects [34].
- Decrease in the dose of the drug formulation [34].

4. HERBAL MEDICINE IN DENTISTRY

4.1. Phytodentistry Aloe vera.

The chemical constituents in Aloe vera are Anthraquinones, Saccharides, Prostaglandins immune modulating, antiseptic, anti- inflammatory. Aloe vera is used in the sites of periodontal surgery, toothpick injuries, chemical burns, aphthous ulcers, gum abscesses, dry socket, lichen planus, benign pemphigus and gingival problems associated with AIDS, leukemia, migratory glossitis, geographic tongue and burning mouth syndrome, denture sore mouth, candidiasis, desquamative gingivitis, vesiculobullous diseases, acute monocytic leukemia, xerostomia.Studies have shown it might lead to allergic reactions: generalized eczematous and popular dermatitis (from topical application) [77, 78].

4.2. Black Cohosh (Rhizoma Cimicifugae).

The main ingredients are cycloartenol-based triterpenes action, acetylacteone, 26 deoxy acetol, cimidenol, 26-deoxyactein and cimicifugaside.It mainly has an anti-inflammatory effect. Studies have been conducted using its anti-inflammatory property in treating periodontitis, but there is a lack of evidence. It is contraindicated in pregnancy or lactation, or in children under the age of 12 years. Minor gastrointestinal upset and headache are some of the adverse effects of black cohosh. Dosage - daily dosage: 40-60% isopropyl alcohol or ethanol extracts of the crude drug corresponding to 40 mg drug [79].

4.3. Bloodroot (Sanguinaria canadensis).

The principal chemical constituent is sanguinarine. It has antibacterial, anti-inflammatory, antifungal property. Mainly used for gingivitis and periodontal disease, remineralization of enamel lesions, acute sore throat. It is considered unsafe for use in children and pregnant or lactating women. Long-term use might lead to nausea and vomiting, glaucoma, edema, heart disease, miscarriage, diarrhea, stomach pain, visual changes, and paralysis [80].

4.4. Caraway (Carum carvi).

Caraway contains 3-7% volatile oil, with the main components divided into carvone (50-60%) and limonene (40%).Some of the properties of caraway include antihistaminic, antimicrobial, antiseptic, expectorant, anti-inflammatory, spasmolytic, flavoring agent.Literature has documented its use in gingivitis, periodontal disease, but definite evidence is lacking. Caraway is not used in children under 2 years of age. Some of the adverse effects reported are irritation of the skin and mucous membrane (Taheri et al., 2011).

4.5. Chamomile (Matricaria recutita).

The Chemical constituents in chamomile are 1-2% volatile oils, essential oil (0.4-1.5%), chamazulene (1 15%). Other major constituents include α-bisabolol and related sesquiterpenes, flavonoids, apigenin, luteolin, and quercetin. These active ingredients contribute to its anti- inflammatory, antispasmodic, smooth-muscle relaxing action, antibacterial and antiviral activity. Major uses are in gingivitis, periodontal disease and ulcers as a mouth wash. Usually considered to be safe during pregnancy or breast-feeding. It is not used in people with allergies to plants of the Asteraceae family (ragweed, aster, and chrysanthemums), as well as mugwort pollen. Bronchial constriction with systemic use and allergic skin reactions with topical use are the other undesirable effects [81].

4.6. Clove Oil (Syzygium aromaticum).

Clove consists of essential oil, eugenol, eugenol acetate and β-caryophyllene. It has analgesic, antibacterial, antiviral, anti-inflammatory, antioxidant property. It has been used to relieve toothache, in periodontitis, as an anesthetic and also to treat bleeding gums. For children, pregnant and lactating women, there is high risk of ill effects.. It is available as a tincture (1:5, 25% ethanol), lozenges and mouthwash [82].

4.7. Cranberry (Vaccinium macrocarpon).

It consists of polyphenols, flavonoids that have anticarcinogenic, antibacterial, antiviral, antifungal, and antioxidant properties. Because of its antiadhesive property dental caries, periodontal disease, oral squamous cell carcinoma. There is no evidence of contraindications and adverse effects [83].

4.8. Dandelion (Taraxacum officinale).

Dandelion has anti-inflammatory, analgesic, antiulcer, antimicrobial property that makes it useful in periodontitis. Contraindications are for those with obstruction of the biliary or intestinal tract and acute gallbladder inflammation, there are chances of minor gastrointestinal upset and headache on long term usage.

4.9. Elderberry (Sambucus arborescent Gilib).

Elderberry consists of flavonoids, major secondary metabolites include about 1% triterpenes, 1% sterols, about 3% phenolic acids and their corresponding glycosides, and up to 0.15% essential oil. The anti-inflammatory activity of its constituents has been made and used to treat periodontitis [82].

4.10. Evening Primrose (Oleum oenothera biennis).

Chemical constituents primrose are linoleic acid (cis-linoleic acid) (65-80%), g-linolenic, acid (cis-g-linolenic acid) (8-14%), oleic acid (6-11%), palmitic acid (7-10%) and stearic acid (1.5-3.5%).Other constituents include sterols and triterpene alcohols. These have antiallergic activity, antiulcer activity. Used in orthodontic tooth movement and dental caries. Some of the adverse effects are headaches, nausea, loose stools and diarrhea. Administration of the fixed oil precipitated symptoms of undiagnosed temporal lobe epilepsy in schizophrenic patients taking phenothiazine [77].

4.11. Garlic (Allium sativum).

Garlic consists of alliin, ajoene, diallyl sulfide, dithiin, S-acetylcysteine, and enzymes, B vitamins, proteins, minerals.It has got antibacterial, antiviral, and antifungal, antiseptic, bacteriostatic, antihelminthic effects. Studies have been done

using garlic to treat dental caries and periodontitis.Reports have shown adverse effects such as allergic reactions such as contact dermatitis and asthmatic attacks, increased bacterial attachment to orthodontic wires [77, 82].

4.12. Ginger (Zingiber officinalis).

The various components of ginger are 1-4% essential oil and an oleoresin, zingiberene, curcumin, sesqui- phellandrene, bisabolene. Monoterpene aldehydes and alcohols are also present.It has antibacterial, anti-inflammatory, analgesic property. It is used to relieve toothache, as a sialogog, in the treatment of oral thrush. Ginger may reduce the toxic effects of the chemotherapeutic agent cyclophosphamide. It should not be used in pregnancy and patients with the biliary disease. Because ginger can interfere with blood clotting, it should be used cautiously in patients on anticoagulant therapies such as cou madin or heparin [82].

4.13. Ginseng (Radix Ginseng).

Chemical constituents of ginseng include triterpene, saponins, oleanolic acid. It is antihelminthic, analgesic, antispasmodic, antimicrobial, anti-inflammatory, antipyretic, immunostimulatory, antiulcer property and used in periodontitis.Adverse effects with its use are hypertension, nervousness, irritability, diarrhea, skin eruptions, and insomnia [84].

4.14. Goldenseal (Rhizoma Hydrastis).

Chemical constituents present are isoquinoline alkaloids principally hydrastine, followed by berberine, canadine and lesser quantities of related alkaloids including Canada line, coalmine, hydrastine and jatrorrhizine.It has got anti-inflammatory and hemostatic property and used in periodontitis. Goldenseal contraindications include those with obstruction of the biliary or intestinal tract and acute gallbladder inflammation. Long term usage might result in exaggerated reflexes, convulsions, paralysis and death from respiratory failure [80].

4.15. Green Tea (Camellia sinensis).

Green tea contains polyphenol contents comprising catechin (C), epicatechin (EC), gallocatechin (GC), epigallocatechin (EGC) epicatechin gallate (ECG), and epigallocatechin gallate.It is anti-inflammatory, antibacterial, antiviral.Used in the treatment of periodontal disease [85].

4.16. Haritaki (Terminalia chebula).

The chemical constituents of Triphala consist of tannins, chebulaic acid, chebulinic acid, cerulenin, corilagin, gallic acid, gallic acid methyl ester, punicalagin, terchebulin and terminalic acid. Flavonols of interest include quercetin, isoquercitrin and rutin.It has antioxidant, antimicrobial, antihelminthic, astringent, dentifrice, anti- inflammatory. Studies have indicated it can be effectively used in the treatment of dental caries, bleeding and ulcerated gums.Contraindicated in children under 12 years, pregnant and lactating women.Daily dosage: 3-9 g of crude drug for decoction in divided doses [86].

4.17. Liquorice (Glycyrrhiza glabra).

Major (29%); minor components occur in proportions that vary depending on the species and geographical location. Glycyrrhizin occurs as a mixture of potassium and calcium salts. Flavonoid constituents include liquiritigenin and isoliquiritigenin. It had antimicrobial, anti-inflammatory and antiviral activity and used in dental caries.Contraindicated in patients with hypertension, cholestatic disorders or cirrhosis of the liver, hypokalemia, or chronic renal insufficiency, and during pregnancy. Some of the adverse effects reported are pseudo aldosteronism, which includes potassium depletion, sodium retention, edema, hypertension, and weight gain. 10 components in liquorice are triterpene saponins, glycyrrhizin (is the major component).

4.18. Myrrh (Commiphora molm).

The three main constituents of myrrh are the resin, the gum, and the volatile oil. The gum consists of 20% proteins and 65% carbohydrates made up of galactose, 4-O-methylglucuronic acid and arabinose. Myrrh had been used in pharyngitis, tonsillitis, gingivitis, stomatitis and ulcers. Topical application for the treatment of and for local application as an anodyne to treat infections of the oral cavity.It should not be used in pregnancy. Adverse effects include contact dermatitis [85].

4.19. Neem (Azadirachta indica).

Neem consists of genin, sodium nimbinate, salannin, nimbin, azadirachtin, nimbidiol, quercetin and nimbidin. Neem leaves contain fiber, carbohydrates and at least 10 amino acid proteins, calcium, carotenoids, fluoride.Neem has antiviral, antifungal, antimicrobial, antibacterial, antipyretic, anti-inflammatory, antitumor, analgesic, antihelminthic, anticariogenic, antioxidant activity. Studies have shown that neem is used in the treatment of dental caries, gingivitis, periodontitis.Dosage - Infusion (1:20): 15-30 ml; Tincture (1:5): 4-8 ml. External applications: 70% ethanol extract of the leaves diluted to 40%, apply twice daily [80].

4.20. Peppermint (Mentha piperita).

Peppermint leaves yield approximately 0.1-1.0% volatile oil that is composed primarily of menthol (29-48%) and menthone (20-31%). It is analgesic and also has muscle-relaxing action. Peppermint oil is applied for toothache by soaking a cotton ball in the oil and placing it in the cavity or rubbing it on the tooth. It is avoided by people with severe liver damage, inflammation of the gallbladder or obstruction of bile ducts though. Adverse effects reported are burning and gastrointestinal upset, skin rashes, headache, heartburn, perianal burning, bradycardia, muscle tremors and ataxia [82].

4.21. Propolis.

Propolis is a complex mixture made up of plant- derived and bee released compounds. Raw propolis consists of around 50% resins, 30% waxes, 10% essential oils, 5% pollen and 5% of various organic compounds. Caffeic acid phenanthryl ester, polyisoprenylated benzophenone, galangal, pino banksin and pino cembrin, amino acids, phenolic acids, phenolic acid esters, flavonoids, cinnamic acid, terpenes.It has got a wide range of activity as anesthetic, antibacterial, antifungal, antiviral (including anti-HIV-1 activity), antioxidant, anticarcinogenic, antimutagenic, antithrombotic and immunomodulatory. It has been used in dental caries, gingivitis, storage medium, intracanal medicament, dentinal hypersensitivity, relief from denture ulceration, stomatitis, halitosis, mouth freshener, periodontal pocket/abscess, dentinal sensitivity, lichen planus, candidal infections, angular cheilitis,

xerostomia, traumatic ulcers, pulp capping, temporary restorations and dressings, covering tooth preparations, dry socket, pre-anesthetic, and pericoronitis [77].

4.22. Purple Coneflower (Echinacea).

It consists of alkyl amides⁄polyacetylenes, caffeic acid derivatives, and polysaccharides. The mouthwash of Echinacea is effective in gingivitis and periodontal disease in combination with sage, peppermint oil, menthol and chamomile. It is ontraindicated in serious conditions such as tuberculosis, leukosis, collagenous, multiple sclerosis, AIDS, HIV infection and autoimmune disorders. It might lead to allergic reactions [77].

4.23. Rosemary (Rosmarinus officinalis).

Chemical constituents of rosemary includes volatile oil, carnosol, ursolic, linalyl acetate (25-46%), linalool (20-45%), lavendulyl acetate (>1.0%), 1,8-cineole, eucalyptol (<2.5%), 3-octanone (<2.5%), camphor (<1.2%), limonene (<1.0%), and α-terpineol (<2.0%).It has antibacterial, antifungal, antioxidant, anti-inflammatory property. It is widely used in relieving toothache, disinfecting GP cones, while contraindicated in pregnant and lactating women. Dosage - Tea can be taken several times per day. Rosemary tincture, half to one teaspoon (2-5 ml) three times per day, may also be used [82].

4.24. Sage (Salvia officinalis).

The volatile oil of sage contains the constituent alpha and beta-thujone, camphor, and cineole. It also contains rosmarinic acid, tannins and flavonoids. It is used in treatment of sore throat, inflammations in the mouth, and gingivitis. Sage oil has antibacterial, antifungal, and antiviral activity that may partially explain the effectiveness of sage for this indication. Not used in pregnant women, children, should be avoided when fever is present. Adverse effects include increased heart rate and mental confusion. Very high amounts may lead to convulsions [77].

4.25. Thyme (Thymus vulgaris).

The primary constituents are the volatile oils, which include the phenols, thymol and arvacrol. A salve made up of thyme, myrrh, and goldenseal is used to treat oral herpes. Also, thyme is used to treat chronic candidiasis and halitosis. It is to be used with caution in young children, pregnant and lactating mothers. Adverse effects include dizziness, vomiting, and breathing difficulties. Some people may be sensitive to use of thyme oil topically on the skin or as a mouth rinse [77].

4.26. Turmeric (Curcuma longa).

Chemical constituents of turmeric include volatile oil (6%) composed of a number of monoterpenes and sesquiterpenes, including zingiberene, curcumin,α- and β-turmerone among others. The colouring principles (5%) are curcuminoids, 50-60% of which are a mixture of curcumin, mono des methoxy curcumin and bis des methoxy curcumin.It is antimutagenic, anticarcinogenic, antioxidant, antibacterial and used in dental caries, oral lichen planus, gingivitis, halitosis, pit and fissure sealant, dental plaque detection system. Massaging the aching teeth with roasted, ground turmeric eliminates pain and swelling [87].

4.27. Tulsi (Ocimum sanctum).

Tulsi consists of tannins (4.6%) and essential oil (up to 2%), eugenol (up to 62%), methyleugenol (up to 86%), and α- and β-caryophyllene (up to 42%), methylchavicol, linalool and 1,8-cineole. It has got antihelminthic, analgesic, antipyretic, immune stimulatory, antiulcer, antimicrobial, anti-inflammatory property. Used in eriodontitis. Contraindicated in pregnant and lactating women, used with caution in children [81].

4.28. Triphala.

Triphala is a riboflavin and niacin. It comprises β-sitosterol, gallic acid, ellagic acid, ethyl gallate, galloyl glucose and cheb Ula gic acid, Haritaki contains chebulagic and chebulinic acid, as well as corilagin. It is antioxidant, antimicrobial. Used in dental caries, bleeding and ulcerated gums [88].

4.29. Other herbs that are useful in dentistry.

Alfalfa: Useful in cases of hemorrhaging and fungal infections [77].

Anises: An anticombination of amalaki, haritaki and bibhitaki. Amalaki contains ascorbic acid, thiamin, -inflammatory herb, anise is commonly used in tea form to soothe the gums [77].

Catnip: Catnip tea or capsules help in relaxation before dental treatment [82].

Cayenne: Cotton with oil of cayenne to aching tooth provides emergency relief from pain[82].

Comfrey: Used as a compress to ease jaw tension and relieve the pain of jaw and tooth fractures [82].

Table 1. The use of medicinal plants for dental treatment [89].

S. No.	Plant name (Common name)	Family	Uses	Partused	Reference
1.	Abuta grandifolia (Mart.) Sandwith (Abota)	Menispermaceae	Toothache	Leaves,bark, Stems & roots	Gupta, 2006
2.	Acacia modesta Wall. (India phulai)	Mimosaceae	To clean teeth	Twig & Stem	Mahmood et al., 2005; Ahmad et al., 2009
3.	Acacia nilotica (L.) Delile (Egyptian Acacia)	Mimosoideae	Swollen gum (gingiviti)	Bark	Shekhawat and Batra, 2006
4.	Acalypha indica L. (Indian copperleaf)	Euphorbiaceae	Toothache	Whole plant	Siddamallayya, 2010
5.	Achyranthes aspera L. (Devil's horsewhip)	Amaranthaceae	Toothache	Leaves and roots	Mahmood et al., 2005; Ahmad et al., 2009
6.	Adansonia digitata L. (Baobab)	Bombacaceae	Toothache	Bark	Dweck, 1996; Burkill, 1985
7.	Alchornea cordifolia Mull.Arg (Lporuru)	Euphorbiaceae	Toothache	Whole plant	Zapfack, 2001; Kayode and Omotoynibo,
8.	Allium sativum L. (Ajo)	Liliaceae	Toothache	Bulb	Gupta, 2006

S. No.	Plant name (Common name)	Family	Uses	Partused	Reference
9.	Aloe ferox Mill. (Aloe)	Liliaceae	Toothache	Leaves	Gupta, 2006
10.	Aloe vera (L.) Burm.f. (Indian Aloe)	Asphodelaceae	Gingivitis & plaque	Whole plant	De Oliveira et al., 2008
11.	Anacardiun occidentlae L. (Acajuba occidentalis)	Anacardiaceae	Toothache, Sore gum	Whole plant	Kayode and Omotoynibo, 2009
12.	Annona senegalensis Pers. (Wild custard apple)	Annonaceae	Toothache	Bark	Mabogo, 1990
13.	Argemone maxicana Linn. (Mexican poppy)	Papaverceae	Toothache and carriage	Seeds	Sikdar and Dutt, 2008
14.	Aristolochia Guentheri O.C. Schmidt (Zaragosa)	Aristolacaceae	Toothache	Stem	Gupta, 2006
15.	Azadiarchta indica A. Juss. (Neem)	Meliaceae	Toothache	Whole plant	Siddamallayya, 2010; Albandar et al., 1997
16.	Baptisia australis (L.)R. Br. (Blue Wild Indigo)	Fabaceae	Toothache	Root	Indiana Medical History Museum, 2010
17.	Blighia sapida K.D.Koenig (Akee)	Sapindaceae	Mouth rashes	Whole plant	Kayode and Omotoynibo, 2009
18.	Borassus flabillifer Linn. (Panai)	Arecaceae	Toothache	Root, Young Rachis	Ganesan, 2008
19.	Bridelia ferruginea Benth. (Kizni)	Euphorbiaceae	Mouth rashes	Whole plant	Kayode and Omotoynibo, 2009
20.	Brugmansia aurea Lagerheim (Floripondio)	Solanaceae	Toothache	Flowers	Gupta, 2006
21.	Cajanus cajan (linn.) Millsp. (Thuvarai)	Fabaceae	Gingivitis	Leaves, stem, seeds	Ganesan, 2008
22.	Calotropis gigantea (L) R.Br. (Akon)	Asclepidaceae	Toothache	Roots	Sikdar and Dutt, 2008
23.	Capparis spinosa L. (Caper bush)	Capparaceae	Toothache	Root bark	Ahmad, 2007
24.	Cassia occidentalis L. (Fedegoso)	Leguminosae	Toothache	Leaves	Agbovie et al., 2002
25.	Cinnamomum camphora L. (Camphor tree)	Lauraceae	Toothache, Teeth swelling	Leaves and branches	Gupta, 2006, Ahmad et al., 2009
26.	Circuma longa Linn. (Turmeric)	Zingaberaceae	Toothache,Gingivitis	Rhizomes	Chaturvedi, 2009
27.	Cleome chelidonii Linn.f. (Perunaikaduku)	Cleomaceae	Gingivitis	Whole plant	Ganesan, 2008
28.	Clitoria ternatea L. (Butterfly pea)	Fabeaceae	Toothache	Roots	Siddamallayya, 2010
29.	Cocos nucifera Linn. (Coconut palm)	Arecaceae	Toothache	Fruits	Dweck, 1996; Spoerke, 1990
30.	Cornus florida L. (Dogwood tree)	Cornaceae	To clean teeth	Stem	Indiana Medical History Museum, 2010
31.	Croton Menthodorus Benth. (Chala)	Euphorbiaceae	Toothache	Seeds, leaves	Gupta, 2006
32.	Datura stramonium Linn. (Dhatura)	Solanaceae	Toothache	Roots	Sikdar and Dutt, 2008
33.	Dialium guineense Wild. (Velvet tamarind)	Leguminosae	Toothache	Root	Agbovie et al., 2002
34.	Ekebergia senegalensis A Juss. (Cape ash)	Meliaceae	Toothache	Leaves	Agbovie et al., 2002
35.	Eruca sativa Miller (Rocket)	Cruciferae	Toothache	Leaves	Ahmad, 2007
36.	Erythrina lysistemon Hutch. (Coral Tree)	Fabaceae	Toothache	Bark	Mabogo, 1990
37.	Eucalyptus globulus Labill. (Blue Gum)	Myrtaceae	Gum bleeding	Whole plant	Reddy et al., 2010; Nagata et al., 2008; Pack, 1984
38.	Euclea divinorum Hiern (Magic gwarra)	Ebenaceae	Toothache	Bark, Leaves	Hutchings, 1996
39.	Euclea natalensis A.DC. (Large-leaved guarri)	Ebenaceae	Toothache	Leaves	Mabogo, 1990
40.	Eucleapseudebenus E. Meyer ex A.DC. (Black ebony)	Ebenaceae	To clean teeth	Root	Damme, 1922
41.	Fagonia cretica L.	Zygophyllaceae	Toothache	Whole plant	Ahmad, 2007

S. No.	Plant name (Common name)	Family	Uses	Partused	Reference
	(Cretan prickly clover)				
42.	Ferula assafoetida Linn. (Heeng)	Apeaceae	Dental carries	Gum resin	Shekhawat and Batra, 2006
43.	Ficus insipid Willd. (Oje)	Moraceae	Toothache	Latex	Gupta, 2006
44.	Ficus bengalensis L. (Indian fig)	Moraceae	Toothache	Plant juice	Ahmad et al., 2009
45.	Flacourtia flavescens Wild. (Niger plum)	Flacourtiaceae	Toothache	Root	Agbovie et al., 2002
46.	Garcinia cola Heckel. (Bitter kola)	Guttiferae	To clean teeth	Root	Agbovie et al., 2002
47.	Jasminum arborescens Roxb. (Chameli)	Oleaceae	Mouth rashes	Leaves	Shekhawat and Batra, 2006
48.	Jasminum officinale L. (Jasmine)	Oleaceae	Mouth rashes	Flower	Siddamallayya, 2010
49.	Jatropha curcas Linn. (Arandi)	Euphorbiaceae	Pyorrhoea	Fruit	Kayode and Omotoynibo, 2009
50.	Juglan regia Linn. (Akhrot)	Juglandaceae	To clean teeth	Bark	Shekhawat and Batra, 2006
51.	Justicia adhatoda L. (Malabar Nut)	Acanthaceae	Pyorrhoea	Leaves	Ahmad et al., 2009
52.	Kleinia longiflora DC (Sambokbossie)	Asteraceae	Toothache	Stem	Damme,1922
53.	Licopersicon esculentum Mill. (Tamater)	Solanaceae	Mouth rashes	Fruit	Shekhawat and Batra, 2006
54.	Lophira alata Banks ex C.F.Gaertn (Bongossi)	Ochnaceae	Toothache	Bark	Cousins and Huffman, 2002
55.	Mangifera indica L. (Mango)	Anacardiaceae	Sore gum	Whole plant	Kayode and Omotoynibo, 2009
56.	Micromeria biflora Benth. (English lavender)	Labiate	Toothache	Root	Ahmad et al., 2009
57.	Milicia excels (Welw.) C.C. Berg (African-teak)	Moraceae	Toothache	Bark	Agbovie et al., 2002
58.	Musanga cecropioides R. Br. (Umbrella tree)	Cecropiaceae	Toothache	Bark	Zapfack, 2001
59.	Myrothamnusuifolius Wblw. (Resurrection bush)	Myrothamnaceae	Gum inflamation	Leaves	Damme, 1922
60.	Nicotiana tabacum L. (Tobaco)	Solanaceae	Toothache	Leaves	Agbovie et al., 2002
61.	Ocimum sanctum Linn. (Tulsi)	Lamiaceae	Mouth sores	Leaves	Shekhawat and Batra, (2006)
62.	Olax subscorpoidea Oliv. (Akan-Brong)	Olacaceae	Toothache	Whole plant	Kayode and Omotoynibo, 2009
63.	Olea ferruginea Royle (Wild Olive)	Oleaceae	Toothache	Fruits	Ahmad, 2007
64.	Origanum vulgare L. (Oregano)	Labiateae	Toothache	Whole plant oil	Indiana Medical History Museum, 2010
65.	Orthanthera albida Schinz. (Ana tree)	Asclepiadaceae	To clean teeth	Stem	Damme, 1922
66.	Palisota hirsute (Thunb.) K. Schum. (Akan-Asante)	Commelinaceae	Toothache	Stem, leaves	Cousins and Huffman, 2002
67.	Parinari curatellifolia Planch.Ex Benth (Cork tree)	Chrysobalanceae	Toothache	Bark	Mabogo, 1990
68.	Phylla dulcis (Trev.) Mold (Aztec Sweet Herb)	Verbenaceae	Tooth decay	Leaves	Indiana Medical History Museum, 2010
69.	Polyalthia suaveolens Engl. & Diels (Annickia)	Annonaceae	Toothache	Fruits, roots and leaves	Cousins and Huffman, 2002
70.	Punica granatum Linn. (Anar)	Puniaceae	Mouth sores	Fruit covers	Shekhawat and Batra, 2006
71.	Ricinus communis L. (Castor bean)	Euphorbiaceae	Toothache	Seeds	Damme, 1922
72.	Saccharum officinarum L.	Graminaceae	Strengthens the	Whole plant	Ahmad et al.,

S. No.	Plant name (Common name)	Family	Uses	Partused	Reference
	(Sugar cane)		teeth.		2009
73.	Salvadora Persica L. (Tooth brush tree)	Salvadoraceae	Tooth decay	Whole plant	Ismail et al., 2010; Almas and Al-Zeid, 2004; Almask et al., 2005;Almas 2001
76.	Sanguinaria canadensis L. (Blood root)	Papaveraceae	Tooth lose	Whole plant	Vogel et al., 1978
77.	Scoparia dulcis Linn. (Sarkaraivembu)	Scrophulariaceae	Toothache	Leaves	Ganesan, 2008
78.	Solanum incanum L. (Thorn Apple)	Solanaceae	Toothache	Root	Sikdar and Dutt, 2008; Ahmad, 2007
79.	Solanum panduriforme E.Mey. (Yellow Bitter-apple)	Solanaceae	Toothache	Roots	Hutchings, 1996
80.	Spathodia campanulata Pal. (African tulip)	Bignoniaceae	Toothache	Bark	Agbovie et al., 2002
81.	Spilanthes americana Hieron (Botoncillo)	Asteraceae	Toothache	Whole palnt	Gupta, 2006
82.	Syzygium aromaticum (L.)Merr. (Clove)	Myrtaceae	Toothache	Whole plant	Barnes 2007; Approaches towards Evaluation of Medicinal Plants prior
76.	Sanguinaria canadensis L. (Blood root)	Papaveraceae	Tooth lose	Whole plant	Vogel et al., 1978
77.	Scoparia dulcis Linn. (Sarkaraivembu)	Scrophulariaceae	Toothache	Leaves	Ganesan, 2008
78.	Solanum incanum L. (Thorn Apple)	Solanaceae	Toothache	Root	Sikdar and Dutt, 2008; Ahmad, 2007
79.	Solanum panduriforme E.Mey. (Yellow Bitter-apple)	Solanaceae	Toothache	Roots	Hutchings, 1996
80.	Spathodia campanulata Pal. (African tulip)	Bignoniaceae	Toothache	Bark	Agbovie et al., 2002
81.	Spilanthes americana Hieron (Botoncillo)	Asteraceae	Toothache	Whole palnt	Gupta, 2006
82.	Syzygium aromaticum (L.)Merr. (Clove)	Myrtaceae	Toothache	Whole plant	Barnes 2007; Approaches towards Evaluation of Medicinal Plants prior to Clinical Trials, 2006
83.	Vitis vinifera L. (Grape vine)	Vitaceae	To clean teeth	Plant ash	Indiana Medical History Museum, 2010
84.	Xanthium spinosum L. (Amor seco)	Asteraceae	Toothache	Fruits, leaves, roots	Gupta, 2006
85.	Zanthoxylum alatum D.C. (Timur)	Rutaceae	To clean teeth	Twigs	Mahmood et al., 2005
86.	Zanthoxylum zanthoxyloides (Lam.) Zeprm. (Candlewood Tree)	Rutaceae	Toothache	Whole plant	Kayode and Omotoynibo, 2009
87.	Ziziphus mauritiana Lam. (Ber)	Rahamnaceae	Dental carries	Root	Shekhawat and Batra, 2006

5. NANOSTRUCTURES USED IN DENTISTRY

5.1. Different forms of nanostructures employed in dentistry

5.1.1. Nanoparticles.

Nanoparticles (diameters of between 0.1 nm and 100 nm) of the various compositions represent the most widespread use of nanoscale units in dentistry. Two year clinical results have shown that these are currently being used in RBC restoration [90, 91]. Together with the evolution of nanoparticles for dental composites, sharper focus is being applied to reformulations of interfacial silanes. Nanohybrid RBCs are currently the most ubiquitous example of such technology.

5.1.2. Nanorods.

These serve as a useful tool in restorative context. Some authors have synthesized enamel-prism-like hydroxyapatite (HA) nanorods that have exhibited self-assembly properties [92, 93]. Nanorods could possible contribute to a practical artificial approximation of a naturally-occurring structure like enamel as they are similar to the enamel rods that make up the basic crystalline structure of dental enamel.

5.1.3. Nanospheres.

Nanospheres can be used in a similar fashion like the nanorods in formulating in restorative technology. Specifically, nanosphere assembly in conjunction with the calcium phosphate deposition

and amelogenin nanochain assembly is discussed elsewhere in a restorative context [92, 94].

5.1.4. Nanotubes.

Different types of nanotubes have been investigated for dental applications in a number of interesting directions. Titanium oxide nanotubes have been shown *in vitro* to accelerate the kinetics of HA formation, so as to serve as coatings, which can accelerate bone growth on the surface of the implants. More recently, modified single-walled carbon nanotubes have been shown to improve the flexural strength of RBCs [92, 95].

5.1.5. **Nanofibers.**

Nanofibers have been expored for their potential use in dentistry to generate ceramics containing HA and fluor-HA. Nanofibrillar silicate crystals have also been recently studied in the capacity of reinforcement of dental composites [96]. These nanofibers demonstrated an improvement the physical properties of the composites when added in correct proportions and with uniform distribution [92].

5.1.6. Dendrimers and dendritic copolymers.

Dendrimers are macromolecular compounds that are made up of a series of branches around an inner core [92, 97]. Dendrimers and dendritic copolymers have been studied, although less extensively than other nanostructures, in relation to dental composite applications. Combinations of specific polymers to optimize efficacy of restorative applications have been reported [92, 98].

5.1.7. Nanopores.

Titanium implants are widely used in dental and orthopedic surgery because of favorable mechanical and biocompatible properties. In order to promote the osseointergration of implants, various surface treatments have been proposed. It has been recently shown that Titanium surfaces with nanopores 30 nm may promote early osteoblastic differentiation and consequently, rapid osseointegration of titanium implants [99].

5.1.8. Nanoshells.

They can prove to be beneficial in the treatment of patients suffering from oral cancer. These are miniscule beads coated with gold. By manipulating the thickness of the layers making up the nanoshells, scientists can design these beads to absorb near-infrared light, creating an intense heat that is lethal to cancer cells [100].

Other nanostructures, which have potential applications in other health-care fields and can also prove to be a useful tool in dentistry are follows: 1. Liposomes; 2. Quantum Dots; 3. Fullerenes; 4. Nanowires; 5. Nanobelts; 6. Nanorings; 7. Nanocapsules.

6. FUTURE PROSPECTIVES

All over the world, the research has been going on herbal remedies and natural products. The development of herbal remedies in the dentistry in a number of institutes is being carried out at basic and clinical trial levels. The only requirement is to develop the better systems for the proper delivery of such drugs at the sites and in the whole body in the doses which will not compromise with the existing treatment. Something that would not only give relieve from side effects like toxicity and hypersensitive reactions but also will increase the patient's strength from inside is very much desirable. In the future, the concept of herbal based nanoformulations for dentistry may also fascinate some potential research groups and potentially create attention-grabbing results. Hence, using “herbal remedy” in the nanocarriers will increase its potential for the treatment of oral health care. Many successful examples with experienced evidences are present among us in the direction of nano research. Herbal remedies are also prosperous resources of advantageous compounds holding antioxidants and constituents that can be made use in purposeful foods. This type of collaborative research among the traditional “Herbal remedies” and newer approaches of modern drug delivery system, i.e., “Nanotechnology” may establish attractive therapies to the pharmaceutical in near future that will enhance health of people. It is anticipated that the effectual and valuable relevance of the natural products and herbal remedies being applied with the nanocarrier will enhance the significance of existing drug delivery systems.

7.REFERENCES

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