II. REVIEW OF LITERATURE

The literature pertaining to the study on the **"Synthesis of Eco-friendly Nanogranular Film in Food Packaging using Medicinal Plants and Nanoparticles"** is presented in the following headings:

A. Global Scenario of Diarrheal Illness

B. Need for Green Synthesis of Silver Nanoparticles

C. Role of Selected Medicinal Plants in Green Synthesis

D. Historical and Recent Applications of Silver Nanoparticles

E. Silver Nanoparticles as a Panacea for Diarrheal Illness

F. Antimicrobial and Anticancer Activity of the Nanocoated and Edible Silver Films

A. Global Scenario of Diarrheal Illness

Food borne diarrheal diseases are a major public health problem with high morbidity and mortality rate, i.e below five years of age and among general age group of the people. Sudershan *et al.,* (2012) reported that globally, the food borne outbreak of diarrhea causes 1.8 million deaths is due to contaminated food and water. According to Center for Disease Control and Prevention (CDC, 2011)globally, food borne illness affects 47.8 million people, childrens of 127,839 were hospitalized due to diarrhea and 3037 were poised for death/year. These food borne illnesses cause diarrhea and are easily transmitted through contaminated food and water. Wolfe *et al.,* (2013) elucidate that globally, the mortality rate of children has declined from 9·9 million to 6·3 million children in 2013, showing that all countries have made a great progress in improving child survival in the millennium.Further, Millennium Development Goals (MDG) have claimed to reduce child mortality by two third in 2015, which have been achieved by a few countries.

WHO (2015) reveals that diarrhea is the second leading cause of death in India, producing a mortality rate of 7,60,000 children every year. A survey conducted by UNICEF (2010) reports that in India, only 47 per cent of rural children, below five wash hands after defecation and remaining 53 per cent children, never wash the hands with soap. This is the major cause of diarrhea.

Kumar *et al*., (2012) reports that poor sanitary and unhygienic conditions are important causes of diarrhea affecting the children below five years of age. They easily transmit infections through contaminated water, infected foods in packages, refuse storage, improper faeces disposal and vectors which predispose the children to diarrhea. In addition, lack of hand washing before feeding their children and indiscriminate stool disposal by the mothers are associated with increased risk of diarrheal illnesses.

Lakshminarayanan *et al.,* (2015) describe that 13 per cent of death, occurs due to diarrhea affecting three lakh children every year in India.In India (2012), the mortality rate due to diarrhea affects 11 per cent of children below five years of age. Jayalakshmy *et al.,* (2011) and National Family Health Survey-3 (NFHS-3) state that nine per cent of children below five years suffer from diarrhea. The incidence of acute diarrheal diseases was as low as one episode/child/year in some urban areas of India.

Bassani *et al.,*(2010) report that in India, diarrhea is the third most common cause of death among underfive years of children, accounting for 13 per cent deaths, killing 3, 00,000 children each year. India is making a steady progress in reducing deaths in children, under five with total deaths declining from 2.5 million in 2001 to 1.5 million in 2012. Even though, diarrheal deaths among children under five years have declined, proportionately the mortality rate, due to diarrheal illness still remains high.

Sudershan *et al.,* (2010) elucidate that 1.5 billion people are affected by diarrheal illness, caused by microbial contamination of food, worldwide. In developed countries, 30 per cent of the people suffer from diarrheal illness. In

India, it was observed that the economic cost of the diarrheal outbreaks in Hyderabad for 60 persons was Rs 91, 901/ (US $ 2070 @ 44/ per dollar).

B. Need for Green Synthesis of Silver Nanoparticles

Several research studies have proved that the phytochemical of the medicinal plant extractsare used as a “Functional Foods” in preventing diseases. The phytochemical constituents of medicinal plants, possessing phenols promoteswellbeing and prevents diseases. In addition, other active phytochemical components in medicinal plants such as coumarins,sterols, saponins, lignans, sulfides,polyphenolics, terpenoids,flavonoids, alkaloids, phthalides, carotenoids and curcumins have been identified.

Tajkarimi *et al.*, (2010) proclaimed that synthetic food additives are posing higher toxicity, therefore, an alternate is to adopt natural alternatives of medicinal plants for extending the shelf-life of foods.Forough *et al.,* (2010) elucidate that phytochemical constituents of medicinal plants possessing the antioxidant are responsible for the reduction of metal compounds into nanoparticles. The bottom up approach for the synthesis of nanoparticles is by oxidation/ reduction of phytochemicals. Therefore, green synthesis provides an advancement over the physical andchemical method as it is eco-friendly and cost effective. There is no need to use high pressure, energy, temperature and toxic chemicals and are easily scaled up for large scale synthesis. Elumalai *et al.,*(2010) reported that the medicinal plants have paved the way for the “greener synthesis” of silver nanoparticles with controlled size, shape, stabilization and crystal growth of nanoparticles.

Mie *et al.,* (2014) suggest that the natural sources of plant extracts are excellent green sources of nanoparticles synthesis. Therefore, these nanoparticles are synthesized without using lethal agents and consumption of low energy such as temperature and pressure.Makarov *et al.,*(2014) observed that the silver nanoparticles synthesized from the extracts of medicinal plants contain a variety of metabolites such as phenols, terpenoids, sugars, alkaloids and saponins which play a vital role in the bio reduction of silver ions to silver nanoparticles.

Samir *et al.,* (2013) state that the reduction of nanoparticle suspension produces diversified colors, which may be due to their optical properties. Mulvancy (2013) described that the colour change of Ag nanoparticle solution, which may be due to the excitation of free electrons producing the surface plasmon resonance (SPR) absorption band through vibration of electrons and light waves. Velayutham *et al.,* (2013) opine that green synthesis of silver nanoparticles (plant extracts) are eco friendly, cost effective and are more beneficial than physical and chemical methods of nanoparticles. Therefore, using the extracts of plants is advantageous, when compared to nanoparticle synthesized from chemicals, enzymes and microbes. Tran *et al.,* (2013) report that phytoconstituents of the plant extracts has the potential to bind metal ions to form nanoparticles (capping of AgNPs) to prevent agglomeration, thereby stabilizing the nanoparticle suspension. The biological molecules of plants, which would perform dual functions of AgNPs formation and its stabilization in the aqueous medium.

Hamouda *et al.,* (2010) describe that synthesizing smaller nanoparticles, which would provide larger surface area available for interaction with microbes would show higher bactericidal effect than larger particles. Jones and Hoek (2010) illustrated that antibacterial activity of AgNP mainly depends on pH temperature and $AgNO_3$ concentration, which are inversely proportional to the Ag^+ concentration. Tolaymat *et al.,* (2010) described that the silver nanoparticle by bottom-up approach produced a homogenous suspension by improving the dissolution of silver salt into a solvent, which undergoes the reduction of silver ions to form stable AgNPs, using phytochemicals from plants as a reducing agent to prevent agglomeration of nanoparticles.

Thirunavoukkarasu *et al.,* (2013) describe that the AgNPs are potent against the infectious organisms such as *E.coli* and act as a powerful antimicrobial agents due to the existing functionalized surface. In addition, Mittal *et al.,*(2014) state that the unique properties of AgNPs have the large surface to volume ratio, which would enhance the surface functionalization of the bioactive agents into the bacterial cell, thereby inhibiting the bacterial cells. Chanda (2013) reports that the smaller particles having a larger surface area, would interact effectively showing a strong bactericidal effect than the larger particles. Bindhu *et al.,* (2013) indicate that the concentration of $AgNO_3$, would influence the silver nanoparticle formation.

Magnuson *et al.,* (2013) reveal that globally, several research studies are done in search of novel substances for preventing the microbial growth and to increase the shelf-life of foods. Silva *et al.,* (2013) report that medicinal plants contains bioactive components which are rich in antioxidant and antimicrobial property, considered as superior alternativestosynthetic food additives. Krishnaiah*et al*.,(2011) state that the antioxidant property of medicinal plants is due to redox potential, which causes the quenching reactive species of singlet oxygen capacity to chelate metals to prevent oxidation of foods. Tajkarimi *et al.*, (2010) proclaim that synthetic food additives pose higher toxicity therefore, an alternate is to adopt natural alternatives of medicinal plants for extending the shelf life of foods.

C. Role of Selected Medicinal Plants in Green Synthesis

Jayathilake *et al.,(*2016) report that the burden of diarrheal and other chronic diseases are increasing rapidly. The biochemical and physiological changes in human body are due to the synthesis of free radicals, which lead to oxidative damage, thereby causing the diseases. Nanoparticles are synthesized using medicinal plant extracts because of their phytoconstituents, which possess anticancer, antioxidant, hypolipidemic and hypoglycemic property. The awareness on prevention of diarrheal illness using traditional medicinal plants have increased considerably in both developing and developed countries over the past two decades. In developing countries, like India and China, medicinal plants are widely used as traditional medicine in treating illness among a majority of the population.

Elzoghby *et al*., (2012) state that the treatment of illness through medicinal plants is called as *herbal medicine* using roots, seeds, leaves, berries, bark and flowers for medicinal purposes. India ranks second in herbal medicine, producing

45,000 plant species, in which 15,000 - 20,000 contain the active phytochemical compounds of medicinal values. Krishnaiah *et al*., (2011) state the antioxidant property of medicinal plants is due to redox potential, which quenches the reactive species of singlet oxygen, capacity to chelate metals to prevent diseases.Out of several species, four medicinal plants with lofty health claims in Ayurveda were selected, 2to authenticate some of their beneficial properties – antimicrobial, antioxidant and anticancer potentials.

The botanical description of the selected medicinal plants used in the present study are as follows :

1. *Andrographis paniculata Wall. Ex Nees*

Family : *Acancthaceae*

Habitat :Throughout India from Himachal Pradesh to Mizoram, Assam and all over Southern India

English : Creat

Ayurveda :Kaalmegha, Bhuunimba, Bhuuminimbaka, Vishwambharaa, Yavtikta, Kalpanaatha,Kirata-tikta (var.), Unani- Kiryaat

Siddha / Tamil : Nilavembu

Action :Hepatoprotective, cholinergic, antispasmodic, stomachic, antihelmenthic and blood purifier. It acts well on the liver, promoting secretion of bile and used in jaundice, torpid liver, flatulence, diarrhea of children, coli, strangulation of intestine, splenomegaly, cold and upper respiratory tract infections.

Key Applications : As a bitter tonic, febrifuge and hepatoprotective (Indian Herbal Pharmacopoeia). Kaalmegha, consist of dried leaves and tender shoots, which yield not less than one per cent andrographolide, dexoyandrographolide and other diterpenes. Andrographolide exhibited strong choleretic action, when administered to rats. It induces the bile flow. Andrographolide was found to be almost devoid of anti-hepatitis B virus surface antigen-like activity (when compared to Picroliv). The leaf and stem extracts of Kaalmegha/ Andrographolide given orally, usually did not change blood sugar level of normal or diabetic rats. Alcoholic extract of the plant exhibited antidiarrheal activity against *E.coli* enterotoxins in animal models. Clinical evidence of effectiveness of *Andrographis* in humans is limited to the common cold. Preliminary evidence suggest that it would increase the antibody activity, phagocytosis by macrophages and anti-allergic activity (Natural Medicines Comprehensive Database, 2007). The herb is contraindicated in bleeding disorders, hypotension, as well as in male and female sterility (exhibited infertility in laboratory animals).

2.*Curcuma longa Linn*

Synonym **:** *C.domestica Valeton*

Family **:** Zingiberaceae

Habitat **:** Cultivated all over India, particularly in West Bengal, Tamil Nadu and Maharastra

English **:** Turmeric

Ayurvedic **:** Haridraa,Priyaka, Haridruma, Kshanda, Gauri, Kaanchani, Krimighna,Varavarnini, Yoshitapriyaa, Hattavilaasini, Naktaahvaa, Sharvari

Siddha/Tamil : Manjal

Action: Anti-inflammatory, cholagogue, hepatoprotective, blood purifier, antioxidant, detoxifier, regeneration of liver tissues, antiasthmatic, antitumour, anticutaneous, antiprotozoal, stomachic, carminative and reduces plasma cholesterol. The anitplatelet activity offers protection to the heart, blood vessels and also protects against the DNA damages in lymphocytes.

Key Applications : In dyspeptic conditions recommended as anti- inflammatory. The rhizome contains curcuminoids, mixture is known as curcumin. It consist of four compounds namely phenolic diarylheptanoids, curcumin, monodes methoxycurcumin and volatile oil. This oil contains 60 per cent of tumerones like sesquiterpene ketones, bitter principles, sugars, starch and resin. The curcumin related phenolics possess antioxidant, anti inflammatory, gastroprotective and hepatoprotective activities. The antioxidant activity of curcumin is comparable to standard antioxidant Vitamin C, E, BHA and BHT. It also exhibits anti-inflammatory activity in a variety of experimental models (effects were comparable to those of cortisone and phenyl butazone). When used orally, curcumin prevents the release of inflammatory mediator and which depletes nerve endings of the substance i.e. neurotransmitter of pain receptors.

Curcumin lowers the cholesterol and interferes with cholesterol uptake, converts cholesterol into bile acids and increases the excretion of bile acids via, its choleretic effects. Curcuminoids prevent the increases in liver enzymes like SGOT and SGPT, which validates the use of turmeric as a hepato protective drug in liver disorders. *Curlone*obtained from the dried rhizome is used against hepatitis. Curcumin in turmeric increase the mucin content of the stomach and exert gastroprotective effects against alcohol, stress, drug- induced ulcer formation (Curcumin at a dose of 100 mg/kg weight exhibited the ulcerogenic activity in rats). The ethanolic extracts of the rhizome exhibit the blood lowering activity in alloxan induced diabetic rats. *Piperine* (a constituent of black and long pepper) which enhances the absorption and bioavailability of Curcumin.

3. Leucas aspera Spreng

Family : *Labiatae;Laminceae*

Habitat : Throughout India in cultivated fields, wastelands, roadsides

Ayurvedic : Dronpushpi, Phalepushpaa, Kutambaka

Siddha/Tamil : Thumbai

Folk : Guumaa, Halkusa (smallervar), Tumbaa

Action :Carminative, antihistaminic, antipyretic, febrifuge and antiseptic. Used in jaundice, anorexia, dyspepsia, fever, helminthic, respiratory and skin diseases. Flowers are given with honey for cough and cold to children. Leaves as a juice are used as an external application for psoriasis, chronic skin eruptions and painful swellings. The alcoholic extract of leaves shows antibacterial activity.

The plant contains oleanolic acid, ursolic acid and betasitosterol. The root contains a triterpenoids, leucolactone, sterols, sitosterol, stigmasterol and campersterol.

4.*Glycyrrhiza glabra Linn*

Family : *Papilionaceae; Fabaceae*

Habitat : Native to the Mediterranean regions. Now grown in Punjab, Jammu Kashmir and South India

English : Licorice, Liquorice

Ayurvedic : Yashtimadhu, Madhuyashtyaahvaa, Madhuli, Madhuyashtikaa, Atirasaa, Madhurasaa, Madhuka, Yastikaahva, Yashtyaahva, Yashti, Yashtika, Yashtimadhuka. Klitaka (also equated with Indigofera tinctoria)(Klitaka and Klitanakam were considered as aquatic varieties of Yashtimadhu).

Unani : Asl-us-soos, Mulethid, Rubb-us-soos (extract)

Siddha/tamil : Athimathuram

Action : Demulcent, expectorant, antiallergic, anti-inflammatory, spasmolytic, mild laxative, anti-stress, antidepressive, antiulcer, liver protective, estrogenic, emmengaogue and antidiabetic. It is also used in bronchitis, dry cough, respiratory infections, cataract, tuberculosis, genitourinary diseases, urinary tract infections, abdominal pain, duodenal ulcers, inflamed stomach and mouth ulcer. Also used for adrenocorticoid insufficiency.

Key application: In upper and lower part of the gastrointestinal tract and duodenal ulcers. It also indicates the use of liquorice for bronchitis, chronic gastritis, peptic ulcer, rheumatism, arthritis, anti inflammatory and antiulcer agent. The main chemical constituent of liquorice isabout 2-9 per cent *glycyrrhizin,* a triterpene saponin with low haemolytic index.*Glycyrrhetinic* (glycyrrhetic) acid contributes 0.5–0.9 per cent, aglycone of glycyrrhizin is also present in the root. The other active constituents of liquorice includes isoflavanoids, chalcones, coumarins, triterpenoids, sterols, lignans, amino acids, gums and volatile oils. Hypokalemia is the greatest threat, when liquorice preparations are high in glycyrrhizin and are prescribed for prolonged periods, which causes fluid retention.

The patients placed on a high potassium, low sodium diet and special precautions should be taken for patients with hypertension, cardiac, renal and hepatic diseases. A special liquorice extract known as DGL (De Glycyrrhizinated Liquorice) is used in the treatment of peptic ulcer. Oral liquorice contains *glycyrrhetinic acid*, which are mainly used for the treatment of viral infections, viral hepatitis and common cold. Topical preparations that contains glycyrrhetinic acid, are mainly used for psoriasis and eczema. In Japan, a preparation of glycyrrhizin, along with cysteine and glycine is also used as an injection for the treatment of acute and chronic hepatitis.

D. Historical and Recent Applications of Silver Nanomaterials

Silver is a rare but naturally occurring metal, often found deposited as a mineral ore in association with other elements. It is usually found in ores with less rare metals like copper, lead, zinc and was apparently discovered in nugget form called as native silver. It is also found in ores containing arsenic, sulphur, antimony and chlorine such as argentite, horn silver, chlorargyrite and pyrargyritein. It was also reported that the ionic silver have been used for centuries as an antimicrobial agent and forms less toxic byproducts compared to other metals (Jones and Hoek, 2010).

Su *et al.,* (2009) elucidated that silver in its metallic form, is a ductile material with atomic number 47, atomic weight 107.87, melting point 961.93°C, boiling point 221.2°C and specific gravity 10.50. The most common oxidation state of silver is 1^+, however 2^+ (for example in AgF_2), and 3^+ (in $KAgF_4$) are also found. The naturally occurring silver is composed of the two stable isotopes 107 Ag (51.8 per cent natural abundance) and 109 Ag (48.2 per cent). In addition, twenty-eight radioisotopes have been characterized with varying, short half-lives. In the natural environment, silver occurs primarily in the form of the sulfide

(Ag_2S) or associated with other metal sulfides, especially those of lead, copper, iron, and gold which are all essentially insoluble. Silver is a white, ductile metal occurring naturally in pure form and in ores. The silver salts such as silver nitrate ($AgNO_3$) are soluble in water, but metallic silver is insoluble in water. Some silver compounds are extremely photosensitive, but are stable in air and water, except for tarnishing readily when exposed to sulfur compounds.

According to Industrial Research Assistance Program (iRAP, 2011) proclaimthat the food materials produced through nanotechnology contribute the largest share in worldwide. In 2008, globally, nano enabled food packaging market was 4.13 billion US dollars, which was projected to grow to 7.3 billion US dollars by 2014. Burkhardt *et al.,*(2011) state that usage of nanosilver is increasing due to its physico-chemical properties such as size, surface charge and solubility that would increase the efficacy of antimicrobial properties of the foods. The silver materials with a particle size larger than 100 nm are indicated as bulk silver. The colloidal silver (a colloid consisting of silver particles suspended in liquid) products remain available in many countries as dietary supplements and as homeopathic remedies.

Durner *et al.,* (2011) state that incorporation of silver nanoparticles in dental materials causes the polymerization process, which leads to an increase in elutable substances such as Campho Quinone (CQ), Ethoxylated diMeth Acrylate (BisEMA) and TriEthylene Glycol Dimethacrylate (TEGDMA) which reduce dental carries. It was also observed that the clinical evidence of silver nanoparticles in dentistry are viable agents for preventing and arrest caries both in the primary and permanent dentition. However these are associated with adverse tooth discoloration and irritation. Therefore, nanosilver compounds on tooth decay have been found to be an effective anti-bacterial agent against dental caries. Toy and Macera (2011) noted that the antimicrobial activity of silver nanoparticles in wound dressings, improves wound healing, is highly sustainable with decreased interference with dressings and reduced toxicity with biodegradable polymers.

Restuccia *et al.,* (2010) state that the traditional food packages are meant for protecting food from external influences. The main functions of food packaging involves preventing the deterioration of foods, extending its shelf-life and improving the quality and safety of packaged food. The packaging usually protects the food from environmental factors such as heat, light, moisture, oxygen, pressure, enzymes, microorganisms, insects, dirt and gaseous emissions, which cause the deterioration of foods.

E. Silver Nanoparticles as a Panacea for Diarrheal illness

Hannon *et al.*, (2015) elucidate that the migration of nanoparticles from food packaging material into food are affected by multiple factors such as concentration gradient, temperature, time, material properties, interaction between the nanoparticle and the nature of food.Beltran *et al.*, (2014) reveal that impregnated silver nanoparticles onto food packages posses antimicrobial and barrier properties. In addition, these nanoparticles would enhance the physical properties of polymers like thermal stability, crystallinity, improves the mechanical properties like emulsification, foaming and water binding capacity, thereby extending the shelf life of foods.

Liang *et al.,*(2012) report that the polymer composites incorporating nanoencapsulated substances such as enzymes, catalysts, oils, adhesives, polymers, inorganic nanoparticles, biological cells, flavour and colour enhancers, vitamins, etc which would act as an alternative for antimicrobial application for improving shelf life of food. Dudkiewicz *et al.,* (2011) report that silver nanoparticles used as a nanofilm in storage containers of food packagesare highly effective to increase the shelf life of food products.

WHO (2011) specifies that silver is permitted as a food additive in food colouring(E174) in the European Union. The Joint FAO/WHO Expert Committee on Food Additives evaluated silver in 1977, but did not set an acceptable daily intake. The US EPA (United States Environmental Protection Agency, 2015) derived an oral reference dose (RfD) (i.e. the dose that can be ingested daily for a lifetime without adverse effects) for silver in humans of 0.005 mg/kg/d (i.e.5

µg/kg/d). The daily dose would be equivalent to the human No-Observed-Adverse-Effect Level (NOAEL - 10 g over a lifetime) from the Drinking Water Quality (WHO, 2011).

Emamifar *et al.,* (2010) report that the antimicrobial packages based on metal nanocomposites are synthesized by incorporating metal nanoparticles into polymer films.The high surface area / volume ratio increases the antimicrobial activity of metal nanoparticles. It was also found that nanocoats on food packages extend the shelf life of orange juice. Sekhon (2010) opine that food packages embedded with nanoparticles could alert the consumers when a product is no longer safe to eat. In addition, these nanocaoted food packages would extend the shelf life of foods, by improving the food safety and barrier properties of foods.

F. Antimicrobial and Anticancer Activity of the Nanocoated and Edible Film of Silver onto Food Packages

Silvestre *et al.,* (2011) described that fresh foods like fruits, vegetables, beverages, dairy and bakery products spoil because of oxidation, reduction, and microbial contamination. Therefore, a new preservative technique known as Polymer Nanomaterials Packaging (PNP) as nanocoating or nanolamination is employed. Polymer Nanomaterial for Food Packaging (PNFP) consists of three disciplines known as “Improved PNFP “, “Active PNFP” and “Intelligent PNFP” on the basis of their properties. They can be used separately or collectively depending on their use. Improved PNFP has well defined polymer flexibility, gas barrier properties, temperature and moisture stability while, the latter two express antimicrobial activities and sensitivity. In PNFP, several polymer materialsare used such as Poly Amide (PA), nylons, polystyrene, EthyleneVinyl Acetate (EVA), copolymers, epoxy resins poly urethane, polyolefin, polyimides and Polyethylene Terephthalate (PET), Hydrate Alumina and Silicate.

Arora *et al.,* (2015) illustrate that the nano lamination consists of two or more layers of nanomaterials which are bound to each other and are used for surface coating/ films in food packaging. The edible coating and films are currently used in a wide range of fruits, vegetables, meats, chocolates, candies, and bakery products. The nanocoating and film of silver could serve as a moisture, lipid, gas barriers that improves the oxidation, reduction and antimicrobial activity of coated food packages. Active PNFP food packagings are made to maintain the internal environment of the food by preventing the light absorption and UV. These silver nanocoatings playsan important role in oxygen scavenging, thereby preventing the redox reaction of foods.

Otles *et al.,* (2012) state that hazards from microbial contamination of the food could be prevented by coating of nanoparticles onto food packages. These coatings act as an oxygen trappers, moisture absorbers and antimicrobial sensors. The advantage of silver nanoparticles and its impregnation onto starch as an edible film improves the mechanical, barrier and antimicrobial property. It also preserves the food from deterioration, extending the quality and shelf life of the food and provides barrier to gases such as moisture, etc.

Duncan *et al.,*(2011) describe that nanoparticles are used as an antimicrobial agents in food packages. The most common nanoparticles synthesized from the metal such as titanium dioxide (TiO_2), Zinc Oxide (ZnO), Silicon Oxide (SiO_2), Magnesium Oxide (MgO), gold, silver etc. Among the metals, silver and gold showed a high temperature stability, low volatiling and a high antifungal and antimicrobial effects against various gram positive and negative bacteria. They also report that the microbial resistivity of silver is less than the other antimicrobial agents and that FDA (2014) approves the direct use of silver as disinfectant in commercial water at maximum level of 17 ug/ kg.

Hannon *et al.*, (2015) report that the migration of nanoparticles from food packages into food may be affected by multiple factors such as temperature, time, concentration gradient, material properties, position of the nanoparticles in the packaging material, interaction between the nanoparticle and material, and nature of the food. Kuorwel *et al.*, (2015) studied that the nanocomposites are commonly called ‘active’ food packaging that refers to the controlled release of active substances from the food packaging materials, which act as aoxygen scavengers. Abreu *et al.,*(2015) illustrated that the nanostructured starch based film containing AgNPs showed higher mechanical properties and water affinity. AgNPscomplex with large number of hydroxyl groups of the biopolymer, which would mainly improve the mechanical, gas barrier properties and antimicrobial activity of the film. Sayes and Santamaria (2014) state that the nanocoated polymer with silver corresponding to ≥ 0.1 per cent achieves the required level of antimicrobial activity to eliminate all bacteria within 24 hours.

Cushen *et al.,* (2014) studied that the effect of time and temperature, depend on the migration of silver from polyethylene (PE) nanocomposites to boneless chicken breasts. The migration of silver occurred from 0.003 to 0.005 mg/dm^{2}to chicken. It was also found that Inductively Coupled Plasma Mass Spectrometry (ICPMS) determined that the silver migration from PVC nanocomposite to chicken, usually occurs after 7 and 10 days. and was below migration limits established by the European Union legislation. Furthermore, the highest migration level was achieved from orange juices, followed by apple and bread. Regardless of the food type, the migration of AgNPs was less than its concentration limit of 10 mg/ml (2002/72/EC).

Beltran *et al*., (2014) describes that the barrier properties of edible film incorporated with AgNP, which extend the shelf life of food through antimicrobial property and water vapour permeability barrier. In addition, nanocomposite packaging were found to be more tensile, durable and thermally stable with UV absorbers such as nano-titanium dioxide, iron oxides, silica, alumina to prevent UV degradation of plastic polymer.

Reig *et al*., (2014) illustrates that the AgNP are most commonly used as an antimicrobial agent for food packages are of two types namely organic and inorganic. Organic materials are frequently less stable at high temperatures compared to that of inorganic agents. The inorganic materials such as metal and metal oxides have the ability to withstand the processing conditions. Echegoyen and Nerı´n (2013) studied the migration of silver from AgNP on different types of nanocomposites packages such as LDPE and PP into foods. It was found that silver migrated into food is heat dependent and that acidic food represent the highest migration level. It was also reported that two different migration mechanisms mainly depend on the release of detached silver nanoparticles and dissolution of silver ions upon oxidation. However, Ag migration is well below the maximum migration limits stated by the European Union legislation.

Cozmuta *et al., (*2014)describe that the first nanocomposites used in food packages, which would enhance the barrier properties is nano-clay. It is also been incorporated with nylons, polyolefins, copolymers, epoxy resins, polyurethane and polyethylene terephthalate. The nanobiocomposites combining nanosilver with other materials,enhance both the barrier and antimicrobial properties in food packaging.Mihindukulasuriya and Lim (2014) illustrate that the polymer-based nanocomposites showed better barrier properties than their conventional composite materials. Such nanocomposites are reinforced with small quantities (typically up to 5 per cent by weight) of nanoparticles, which have very high aspect ratios (L >300) and these are incorporated in addition to the traditional fillers and additives.

Fabra *et al.*, (2013) describe that among several polymers, Polypropylene (a type of polyolefin) films are often used because of its transparency, brilliance, low specific weight and chemical inertness. However, polypropylene (PP) is also characterised by low barrier properties (i.e. an inherent permeability to gases and other small molecules), which result in poor protection of packaged foods. One of the methods to improve PP and other plastics barrier deficiencies is to add a second component such as the nanoparticles.

Azeredo *et al.,* (2013) report that nanocomposites are widely used as ‘active’ packaging, which include polymer composites with antimicrobial nanomaterials, such as silver, zinc oxide, magnesium oxide. ‘Active’ packaging is intended to enhance the condition of the packed food, extend shelf-life, or improve sensory properties while maintaining the freshness and quality of food. Therefore, the nanosilver in plastics which confers the antimicrobial properties to improve shelf life of foods.

Motlagh *et al.,* (2012) propose that the low-density polyethylene-silver (LDPE-Ag) packages with >1 per cent concentration of Ag nanoparticles preserve the quality and prolong the shelf-life of barberries compared with that of LDPE alone. The AgNPs in LDPE packages were able to maintain the sensory, physicochemical and physiological qualities of barberry and strawberry fruits at a higher level compared with normal polyethylene bags.

Mahdi *et al.* (2012) evaluated the antimicrobial effect of AgNPs incorporated in PVC in minced beef, during storage at refrigerator temperature (4°C). It was observed that the bacterial growth slowed down significantly even after seven days of against *Escherichia coli* growth and *Staphylococcus aureus* growth, which allowed an increased shelflife of minced meat that usually spoils after two days of storage in common food packaging.

Cushen *et al.,*(2012) propose that the silver as AgNP is well-known for its wide-ranging antimicrobial activity against gram positive and gram negative bacteria, fungi and viruses. Due to the incorporation of Ag into a variety of polymers, have proved to be an effective antimicrobial agent. Lloret *et al.,* (2012) studied that the microbial growth, enzyme and water activity are the most important factors, which affect the quality of fresh fruit and vegetables. It was also observed that Ag nanoparticles in cellulose material act as an antimicrobial packaging, in which the meat and fruit samples were stored upto 10 days without spoilage.The total viable count of microorganisms, yeasts and moulds in kiwi and melon juices were reduced by 99.9 per cent. The total viable count and lactic acid bacteria in drips from poultry and beef samples stored in nanocomposite packaging were consistently 90 per cent below that of the controls.

Chamorro *et al.,* (2011) propose that the most commonly used polysaccharides is starch used in preparation of edible film. Among the non-degradable polymers Polyethylene (PE) is the most largely used to host AgNPs for food packaging. It was found that Low-density polyethylene (LDPE) polymer containing Ag nanoparticles have found to extend the shelf life of orange juice and also act as an effective antimicrobial agent in combination with heat treatment at the pasteurization temperature (55 – 65°C). The LDPE with nanosilver are significantly more effective against fungi than the uncoated LDPE covers. The antimicrobial activity of AgNPs in these LDPE covers decreased the pasteurization temperature of orange juice by 10 C. Yang *et al.,* (2010) also studied similar effects by testing Ag LDPE packages in preserving the appearance and sensory quality of stored barberries. Emamifar *et al.,*(2010) revealed the extension of the shelf-life of orange juice samples to 56 days at 4°C, by storing in nanocomposite LDPE films loaded with Ag nanoparticles. The total plate count was significantly decreased in Ag nanocomposite film compared with that of LDPE film.

Mulukuri *et al.,*(2011) report that medicinal plants are increasing all over the world, which promises an immense potential of medicinal plants in treatment of various disorders. World Health Organization (WHO) estimates that 80 percent of the populations of Asian and African countries presently use herbal medicine for some aspect of primary health care. Devi *et al.,* (2014) stated that cancer is the third leading cause of death worldwide, preceded by cardiovascular and infectious diseases. The potential use of silver nanoparticles with the medicinal plants as anticancer agents poses no side effects in healing of cancer.

Saleem *et al.,* (2011) illustrated that the root of licorice of *Glycyrrhiza glabra* are the most commonly used and are referred to as grandfather of herbs. It has been used medicinally in both Western and Eastern countries for more than 4000 years. The biologically active constituents of *Glycyrrhiza glabra*are widely used in cancer treatment of various glands such as respiratory, gastrointestinal, cardiovascular and skin disorders. Zhong et al., (2010) stated that the silver nanoparticles are widely used in eradication of cancer cells by flow and penetration to different regions of tumors through blood vessels and then to interstitial space to arrive at the target cells. The environmental and physiological characteristics vary from one tumor tissue to another. Silver nanoparticles inhibit the proliferation of the cancer cell lines by different mode of actions. Apoptosis of cancer cell by silver nanoparticles is highly regulated and efficient cell death programme.

Stensberg *et al.,* (2011) proclaim that the mechanism of anticancer activity of silver nanoparticles mediates and amplify death signal by triggering the Caspase-3 molecule. The DNA is broken in to fragments by the action of Caspase 3. The silver nanoparticles interfere with the functioning of cellular proteins and induce subsequent changes in cells, which alters the mitochondria by inhibiting the catalytic activity of lactate dehydrogenase. The silver nanoparticles induces the proliferation of reactive oxygen species (ROS) which ultimately leads to DNA damage. Moreover the green synthesized metal nanoparticles lefts less or no side effects on the cancer patients. Lima et al., (2012) described that antitumor activity of the plant mediated silver nanoparticles inhibited the growth of cancer cells. The cytotoxic activity was dose and time dependant with an IC50 of 20μg/ml and 40μg/ml for 24hrs and 48hrs respectively.

Edible Films

Fortuny *et al.,* (2013) illustrate that the greatest hurdle of the food industry is its limited shelf life of food products due to degradation, enzymatic browning and oxidative rancidity. Therefore,it is necessary to reduce food deterioration by using the edible films and coatings. Edible films are thin layers of material, which act as a barrier against different agents such as water vapor, oxygen and moisture) that would improve quality and extend the shelf life of processed foods. The addition of active compounds namely antioxidants to these films, would enhance their functional properties in food preservation.

Akhtar *et al.,* (2012) state that the antioxidant from natural sources namely plant extracts, essential oils, etc are widely used to replace synthetic agents. Pastor *et al.,* (2011) describe that the addition of antioxidants to edible films would enhance the shelf life of fresh-cut fruits, thereby, inhibiting browning and reduce the undesirable effects of nutrients oxidation. The extracts possessing antioxidant property influence the edible film mainly based on (i) properties of the material, which they are being incorporated, such as retention power (ii) the characteristics of the food product like flavor, color and chemical modifications.

Denobili *et al.,* (2013) state that the synthetic antioxidants and antimicrobials have raised some safety concerns and regulatory agencies have restricted their use as food additives. Therefore, as an alternate, natural extracts are used as antimicrobial agents in films. These extracts improve the food quality by preventing food deterioration. Li *et al.,* (2014) show that the plant extracts from medicinal plants possess excellent antioxidant activity that would retard lipid oxidation, by improving the quality and shelf life of foods. The antioxidant activity of these extracts is due to the strong scavenging activity of phenolic compounds, which are able to protect the food products. In addition, these extracts exhibit antioxidant properties, which also act as photo-oxidation through reduced light transmission reduces water activity and moisture.

Pavlath and Orts (2009) report that edible films are thin layers made from silver nanoparticles and starch, which act as a barrier layer to improve the shelf life of foods. These edible films retard the oxidation process, desorption of moisture and prevents the microbial growth and sensory changes by controlling the moisture, oxygen, carbon dioxide, flavour and atmospheric conditions of foods, thereby, enhancing the quality of food products. Cerqueira *et al.,* (2011) state that these edible films are synthesized from materials which are dispersed in solvents such as water, alcohol or a mixture of other solvents. Plasticizers, antimicrobial agents, colors or flavors which could also be added in this process. Galus and Lenart (2013) describe that film thickness is an important characteristic in packaging materials for food products. The thickness of films, which may affect other characteristics of the films such as tensile strength, elongation, and water vapor permeabilityis dependent on both film composition and processing parameters.

Singh *et al.,* (2011) describe that the cross-linking means that polymer molecules are interconnected by bonding such as covalent and ionic which can result from intermolecular forces of hydrogen bonding. Cross-linking is a key technique for modifying the starch properties, which could be achieved by adding intra- and inter-molecular bonds in starch granules. El-Tahlawy *et al.,* (2007) showed that the cross-linking limits the interaction of starch with water, which provides a structural integrity of starch-based biodegradable materials. The starch cross-linking is done by treating starches with reagents capable of forming either ether or ester linkages between hydroxyl (–OH) groups on starch molecules. The biodegradable starch film prepared from cross-linked starch provides improved mechanical properties, resistance to stress cracking and decrease in flexibility.

Das *et al.,* (2010) showed that cross linked starch/PVA blend films had mechanical properties higher than native sago starch/PVA blend films. The increased mechanical properties is due to the increase in cross-linking density. The cross-linking agents react with the -OH groups present in starch, which links the ether linkages with the hydroxyl groups that would increase the mechanical properties. Due to the cross-linking reinforces the structure of starch granules, which limits the water absorption of starch, thereby restricting the mobility of the starch chain in the amorphous region.

Taghizadeh (2013) reported that the silver nanoparticles impregnated in starch film, which usually hinders the diffusion of gases and improves their thermal and mechanical properties.Fadeyibi *et al.,*(2016) reported that developing the nanocomposite films using tapioca starch and AgNPs has found its potential applications in food packaging industry. These films were found to be thermally stable with 2% to 3% of their weights degraded below 100°C, water vapour permeability increased while the oxygen permeability decreased with increased concentration of glycerol and Ag nanoparticles. The lower gas permeability of cassava starch nanocomposite film, which has reduced down the rate of respiration, higher water vapour permeability that retains the keeping quality in packaged foods. In addition, the oxygen scavenging effect of silver nanoparticles, which retards ripening, senescence and deterioration that are responsible for low gas permeability of packaging material.

Majdzadeh-Ardakani *et al.,* (2010), stated that silver nanoparticles incorporated into tapioca starch forming a thin polymeric film containing metal precursor. These nanostructured starch materials have been prepared by solution casting and melt intercalation. Bozani *et al.,* (2011) iilustrated that these starch films with Ag-NPs (7.8 mM) prepared by solution casting, which have been proved to prevent the viability and growth of pathogens such as *Staphylococcus aureus, Escherichia coli* and *Candida albicans*. These starch based nanostructured films possess the high antimicrobial property with improved mechanical and barrier properties.

Marilena Carbone*et al.,* (2016) stated that the growing demand for increased fresh food and longer shelf life of foods against foodborne diseases urged the development of edible films as antimicrobial packaging in food industry. Among the most efficient methods, the combination of organic–inorganic, packaging, i.e. polymer embedded metal nanoparticles proved to be highly effective. Silver nanoparticles (AgNPs) synthesized from plant extracts possess the antimicrobial, anti-fungi, anti-yeasts and antiviral activities that can be combined as both non degradable and edible polymers for active food packaging.

Roshetko *et al*., (2013) illustrated that the antibacterial activity of edible films are derived from the plant extracts which contain the bioactive compounds namely phenol. Due to the addition of leaf extract possessing phenol along with AgNP to the edible films, which would prevent the contamination of food borne pathogens namely *E.coli* and *S. aureus.* Bumbudsanpharoke and Ko (2015) reported that the use of nanomaterials in several fields is growing and also in food packaging. Nanotechnology enabled food packaging can be divided into two different aspects namely (i) improved packaging, were nanomaterials are mixed into the polymer matrix to improve the gas barrier properties such as polymer/ clay nanocomposite (ii) active packaging in which the silver nanoparticles act as a potent antimicrobial agents that would interact directly with the food to increase the shelf life of foods.

Toker *et al.,* (2013) illustrated that metal nanoparticles with their potent antimicrobial properties are therefore used as ‘‘active packaging”. Emerging metal nanoparticles with biocidal properties are Cu, Zn, Au, Ti, and Ag. Among the metals, silver nanoparticles (AgNPs) demonstrated to possess the most effective bactericidal properties against a wide range of pathogenic microorganisms, including bacteria, yeasts, fungi and viruses. AgNPs showed better antimicrobial properties compared to metallic silver thanks to their extremely large surface area which can provide a better contact with the microorganism.