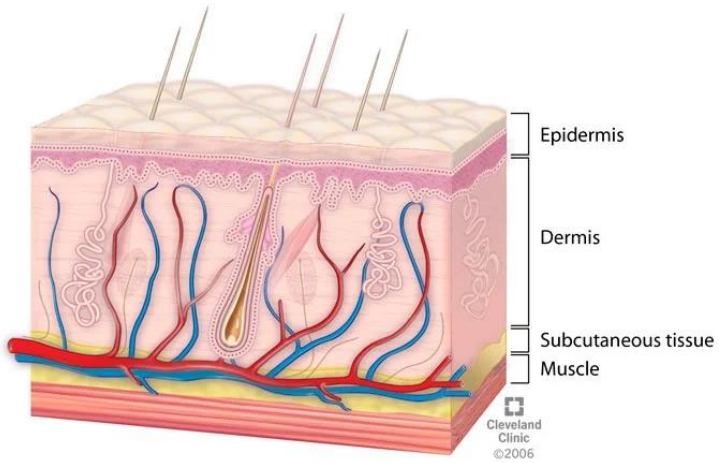
Introduction

PHYSIOLOGY OF HUMAN SKIN

Epidermis The epidermis is the most superficial layer of the skin and is composed of stratified keratinized squamous epithelium, which varies in thickness in different parts of the body. It is thickest on the palms of the hands and soles of the feet. There are no blood vessels or nerve endings in the epidermis, but its deeper layers are bathed in interstitial fluid from the dermis, which provides oxygen and nutrients, and drains away as lymph.1



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Dermis The dermis is tough and elastic. It is formed from connective tissue and the matrix contains collagen fibers interlaced with elastic fibers. Rupture of elastic fibers occurs when the skin is overstretched, resulting in permanent striae, or stretch marks, that may be found in pregnancy and obesity. Collagen fibers bind water and give the skin its tensile strength, but as this ability declines with age, wrinkles develop. Fibroblasts, macrophages and mast cells are the main cells found in the dermis. Underlying its deepest layer there is areolar tissue and varying amounts of adipose (fat) tissue. 1

Subcutaneous gland These consist of secretory epithelial cells derived from the same tissue as the hair follicles. They secrete an oily substance, sebum, into the hair follicles and are present in the skin of all parts of the body except the palms of the hands and the soles of the feet. They are most numerous in the skin of the scalp, face, axillae and groins. 1

CREAMS

The topical products that can be applied to the skin are called creams. In terms of dosage forms, creams are "viscous liquid or semi-solid emulsions of either the oil-in-water or water-in-oil type," whose consistency changes depending on the amount of oil and water present. Creams are used for therapeutic or cosmetic functions such as cleansing, beautifying, improving appearances, protecting, etc. These topical formulations are intended to distribute drugs to specific areas of the skin or mucous membrane for localized effects. These items are made to be used topically for more effective site-specific medicine delivery to the skin for skin conditions.1

Creams are considered as a pharmaceutical product as they are prepared based on techniques developed in the pharmaceutical industry; unmedicated and medicated creams are highly used for the treatment of various skin conditions or dermatoses. Creams can be ayurvedic, herbal or allopathic which are used by people according to their needs for their skin conditions. They contain one or more drugs substances dissolved or dispersed in a suitable base. Creams may be classified as o/w or w/o type of emulsion on the basis of phases. The term ‘cream’ has been traditionally applied to semisolid formulated as either water-in-oil (e.g.: cold cream) or oil-in-water (e.g.: vanishing cream).3

TYPES OF SKIN CREAMS

They are divided into two types:

Oil-in-Water (O/W) creams which are composed of small droplets of oil dispersed in a continuous phase, and an emulsion in which the oil is dispersed as droplets throughout the aqueous phase is termed an oil-in-water (O/W) emulsion.

Water-in-Oil (W/O) creams which are composed of small droplets of water dispersed in a continuous oily phase. When water is the dispersed phase and an oil the dispersion medium, the emulsion is of the water-in-oil (W/O) type.4

CLASSIFICATION OF CREAMS

All the skin creams can be classified on different basis:

1. According to function, e.g. cleansing, foundation, massage, etc.

2. According to characteristics properties, e.g. cold creams, vanishing creams, etc.

3. According to the nature or type of emulsion.5

Evaluation parameters of creams

1. Determination of pH

2. Physical appearance

3. Spreadability

4. Saponification value

5. Acid value

6. Viscosity

7. Homogeneity

8. Removal

9. Dye test

10. Skin hydration test. 5

Types of creams according to function, characteristic properties and type of emulsion:

1. Make-up cream (o/w emulsion): a) Vanishing creams. b) Foundation creams.

2. Cleansing cream, Cleansing milk, Cleansing lotion (w/o emulsion)

3. Winter cream (w/o emulsion): a) Cold cream or moisturizing creams.

4. All-purpose cream and general creams.

5. Night cream and massage creams.

6. Skin protective cream.

7. Hand and body creams.6

Functional	Physicochemical	Subjective
Cleansing Creams	Creams Medium to High oil content	Oily Cold
Cold creams	O/W or W/O	Difficult to 'Rub in'
Massage Creams	Low Slip Point oil phase	May be stiff and rich
Night Creams	Neutral pH	Also popular as lotions
Moisturizing Creams	Low oil content	Easily spreadable and 'Rub in' quality
Foundation Creams	Usually O/W Available	as creams and lotions

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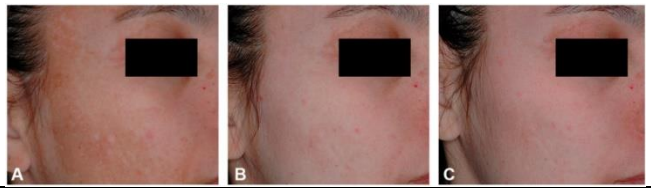
GENERAL INGREDIENTS USED IN SKIN CREAMS : The raw materials which are used in a manufacturing of skin creams include:

- Water:
- Oil, fats and waxes:
- Minerals oil
- Glyceride oil
- Vegetable oil:
- Waxes
- Fats
- Perfumes
- Vitamins 1

combination cream	uses
0.01% fluocinolone acetonide, 4% hydroquinone, 0.05%and tretinoin	used sequentially with intense pulsed light (IPL) treatments in patients with moderate to severe melasma. 
4% hydroquinone, 0.05% Tretinoin and 0.1% mometasone furoate cream with glycolic acid peels	treatment of melasma.
The lipids in the simplified creams were either hydrocarbons or vegetable triglyceride oil, and one of them also contained 5% urea.	treated and control forearms were exposed for 24 h to sodium lauryl sulfate (SLS) using a patch test
Brimonidine 0.2%, Timolol 0.5% in base emollient cream	used for ulcerated IH with re-epithelialization of ulcerated IH
Fusidic acid 2%/ hydrocortisone 1% cream	Mild to moderate infected eczema of the trunk or limbs
Fusidic acid 2%/ betamethasone 0.1% cream	Infected or potentially infected eczema

(8,9,10,11.12,13)

Ointments

An ointments are homogenious, viscous semisolid preparation, most commonly a greasy, oily (Oil-80%, Water-20%) with high viscosity that is intended for external application to skin or mucous membranes. They are used as emollients or for the application of active ingredients to the skin for protective, therapeutic, or prophylactic purposes and where a degree of occlusion is desired. Ointments are used topically on a variety of body surfaces. These include the skin and the mucous membrane of the eye (an eye ointment), chest, vulva, anus and nose.14

Ointment have very moisturizing characteristic and are effective for dry skin. They have very low risk of sensitization due to having few ingredients beyond the base oil or fat and also low irritation risk. They have more greasiness so mostly disliked by patients.14

Types of Ointment:

Ointment may be medicated or non-medicated.

a) Medicated ointment: For the application of API to skin for protective, therapeutic, or prophylactic purpose.

b) Non-medicated ointment: These are used for physical effect. They are use as protectant, emollients, or lubricants.

Characteristics of an ideal ointment

1) It should be physically and chemically stable.

2) In ointment base, finely divided active ingredients should be uniformly distributed.

3) The base of ointment should not possess any therapeutic action.

4) The ointment should be smooth and free from grittiness.14

Advantages of an ointment

1) They have site specific application of drug on affected area, which avoids unnecessary non target exposure of drug thereby avoiding side effect i.e. site specific action with less side effect.

2) They avoid first pass metabolism of drug.

3) Convenient for unconscious patients having difficulty in oral administration.

4) Comparatively they are chemically more stable and easy to handle than liquid dosage forms.

5) They are suitable dosage forms for bitter taste drugs.14

Disadvantages of an ointment

1) These oily semisolid preparations are staining and cosmetically less aesthetic.

2) Application with finger tip may contaminate the formulation or cause irritation when applied. 3) As compared to solid dosage forms, semisolid preparation are more bulky to handle.

4) Though semisolid allow more flexibility in dose, dose accuracy is determined by uniformity in the quantity to be applied.

5) Physico-chemically less stable than solid dosage form. 14

Ointment Bases Ointment bases are generally classified into four groups: (a) oleaginous bases, (b) absorption bases, (c) water-removable bases, and (d) water-soluble bases.

Oleaginous Bases Oleaginous bases are also termed hydrocarbon bases. On application to the skin, they have an emollient effect, protect against the escape of moisture, are effective as occlusive dressings, can remain on the skin for long periods without drying out, and because of their immiscibility with water, are difficult to wash off. Water and aqueous preparations may be incorporated, but only in small amounts and with some difficulty.

Absorption Bases Absorption bases are of two types: (a) Oil-in-Water (O/W) creams which are composed of small droplets of oil dispersed in a continuous phase, and an emulsion in which the oil is dispersed as droplets throughout the aqueous phase is termed an oil-in-water (O/W) emulsion.

Water-in-Oil (W/O) creams which are composed of small droplets of water dispersed in a continuous oily phase. When water is the dispersed phase and an oil the dispersion medium, the emulsion is of the water-in-oil (W/O) type..

Water-Removable Bases Water-removable bases are oil-in-water emulsions commonly called creams. Because the external phase of the emulsion is

aqueous, they are easily washed from skin and are often called water-washable bases. They may be diluted with water or aqueous solutions. They can absorb serous discharges. Hydrophilic Ointment, USP, is an example of this type of base.

Water-Soluble Bases Water-soluble bases do not contain oleaginous components. They are completely water washable and often referred to as greaseless. Because they soften greatly with the addition of water, large amounts of aqueous solutions are not effectively incorporated into these bases. 15

14 Different Ointment Bases

SELECTION OF THE APPROPRIATE BASE Selection of the base to use in the formulation of an ointment depend on number of factors, including the following:

1) Desired release rate of the drug substance from the ointment base.

2) Desirability of topical or percutaneous drug absorption.

3) Desirability of occlusion of moisture from skin.

4) Stability of the drug in the ointment base. 14

5) Effect, if any, of the drug on the consistency or other features of the ointment base.

6) Desirability for easy removal of base by washing with water.

7) Characteristics of the surface to which it is applied.

IDEAL PROPERTIES OF OINTMENT BASES

1) Should not retard wound healing.

2) Have a low sensitization index.

3) Pharmaceutically elegant.

4) Release the medicament efficiently at the site of application.

5) Have a low index of irritation.

6) Non-dehydrating, non-greasy and neutral in reaction.

7) Compatible with common medicaments and also with the skin.

8) Easily washable with water.

9) Have minimum number of ingredients.

10) Easy to compound and remain stable on storage and chemically stable.14

OTHER ADDITIVES IN OINTMENT PRESERVATIVES IN OINTMENT

The antimicrobial compounds and their quantities should be carefully decided upon if the same are to prevent contamination, deterioration or spoilage of ointment bases by bacteria and fungi. The first consideration in selection is the irritancy or toxicity of the compound to the tissue to which the ointment is to be applied. For instance, methyl and propyl parabens are irritant to nasal passages. Boric acid may also get absorbed through the nasal passages in sufficient amounts to be toxic. Quaternary ammonium compounds or phenylmercuric nitrates are better tolerated by nasal tissues.

On occasions the plastic containers or rubber closures may 'take up' some amount of the preservatives thus reducing their availability for antimicrobial action. Sometimes the preservatives get complexed by other ingredients and are thus not available in sufficient concentration for antimicrobial action. In the presence of tween 80, methylparaben, benzalkonium chloride, benzoic acid etc. get inactivated to appreciable extents. The bactericidal activity also depends upon partition coefficient of the antimicrobial compound between aqueous and oily phases. If both the phases are to be protected additional amounts may be needed. Hence, a practical man should make viable counts on his products after a period of storage in order to judge preservative qualities of the antimicrobial compounds used. ANTIOXIDANTS IN OINTMENT Antioxidants should be included to avoid the oxidative degradation of the base. It may be more desirable to select two antioxidants instead of one. The concentration of antioxidants depend upon their partition coefficients between the aqueous and oil phases if both the phases are present in a base. Generally compounds like butylated hydroxy anisole, propyl gallate, nor dihydroguaiaretic acid etc. are used in ointment bases. CHELATING AGENTS Whenever it is anticipated that traces of metallic ions are likely to catalyse oxidative degradations small amounts of substances such as citric acid, maleic acid, phosphoric acid etc. may be added to chelate the metallic ions.

PERFUMFES Most ointments have a pleasant smell imparted by incorporation of selected perfume blend. The selection of a perfume blend is a very criticle. The blends selected must be compatible with other ingredients. Essential oils from plant materials used as perfumes. The floral group blends such odours as jasmine, rose, lily and gardenia. The woody is group characterize by sandal wood, cedar wood.

HERBAL OR PLANT MATERIALS Human beings have been using herbs (plants) for different purposes like food, medicine, beatifying.In good old days many herbal and natural materials used to be employed for beauty treatment. Gradually with the advancement of science, readymade cosmetic preparations came into existence. Today variety of chemical substances of

different origins are used in cosmetics There is resurgence of use of herbal ingredients in creams. 14

METHOD OF PREPARATION OF OINTMENT

Preparation of ointment mainly depend on nature of ingredients. Ointments are mainly prepared by two general method:

a) Incorporation b) Fusion

a) Incorporation In this finely subdivided insoluble medicaments are evenly distributed by grinding with a small

amount of the base followed by dilution with gradually increasing amounts of the base

Mortal And pestle

b) Fusion In this method the ingredients are melted together in descending order of their melting points and stirred to ensure homogeneity. 14

EVALUATION PARAMETERS OF OINTMENT The different methods of evaluation of ointment are

(1) Physical methods : Test of rate of absorption ,Test of non-irritancy ,Test of rate of penetration , Test of rate of drug release , Test of rheological properties ,Test of content uniformity

(2) Microbiological methods : Test of microbial content ,Test of preservative efficacy.14

Plant Profile

Plant Extract	Aloe Vera	Hibiscus	Senna
			
Synonym	Aloe ferox, Cape aloe	Mahoe, Shoeblack plant, Mahagua	Alexandrian senna, Sonamukhi
Active constituents	Vit,minerals, enzymes, Sugars, lignin, saponins Amino acids,98%water	Anthocyanins, polyphenols Flavonoids,15-30%plant acid e.g.citric,malic acid	Glycosides, sennosides C and D Monoanthrones, Dianthrones
uses	Anti – infflamatory Moisturizes the skin, heals burns	Anti – bacterial,glowing skin,cleansing pores.	Nourishes skin cells,laxatives and carminative.

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Different between cream and ointment

Feature	Creams	Ointments
Appearance	Usually white to off-white	Usually translucent
Nature of Formulation	Water-based semisolid preparation.	Oil-based semisolid preparation.
Constituents	More than 20% water and volatiles and normally less than 50% hydrocarbons, waxes, or polyols as the vehicle.	Less than 20% water and volatiles, and more than 50% hydrocarbons, waxes, or polyols as the vehicle.
Viscosity	Thin	Thick
Spreadability	Easily spreadable.	Less easily spreadable.

Greasiness	Non-greasy or less greasy	Greasy
Absorption	Faster	Slower
Duration of action	Short	Prolong
Shelf-life	Shortened	Longer
Stains on clothing	No chance	Have a chance
Wash off	Easier	Less easy
Example	Betamethasone Valerate Cream, Zinc Acetate 0.2% cream, and Econazole Nitrate cream etc.	Hydrocortisone Ointment, Bacitracin and Lidocaine ointment etc.

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Nanoparticle

Nanoparticles are defined as particulate dispersions or solid particles with a size in the range of 10-1000nm. 18

Nanoparticles exist in various chemical compositions ranging from micelles to metal(oxide)s, from synthetic polymers to large biomolecules. Each of these materials features a completely different chemistry, which can be analyzed by a variety of methods including optical spectroscopy, X-ray fluorescence and absorbance, Raman spectroscopy, and solid-state NMR. 19

Classification of Nanoparticles

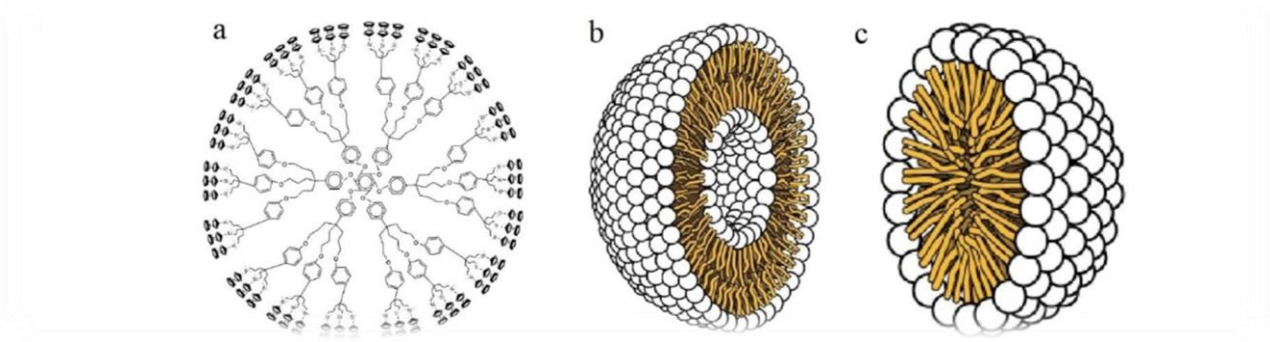
The nanoparticles are generally classified into the organic, inorganic and carbon based.

Organic nanoparticles

Dendrimers, micelles, liposomes and ferritin, etc. are commonly knows the organic nanoparticles or

polymers. These nanoparticles are biodegradable, non-toxic, and some particles such as micelles and

liposomes has a hollow core (Figure1), also known as nanocapsules and are sensitive to thermal and electromagnetic radiation such as heat and light.These unique characteristics makes them an ideal choice for drug delivery. The drug carrying capacity, its stability and delivery systems, either entrapped drug or adsorbed drug system determines their field of applications and their efficiency apart from their normal characteristics such as the size, composition, surface morphology, etc. The organic nanoparticles are most widely used in the biomedical field for example drug delivery system as they are efficient and also can be injected on specific parts of the body that is also known as targeted drug delivery.20



Organic nanoparticles: a – Dendrimers, b – Liposomes and c – micelles.

Inorganic nanoparticles

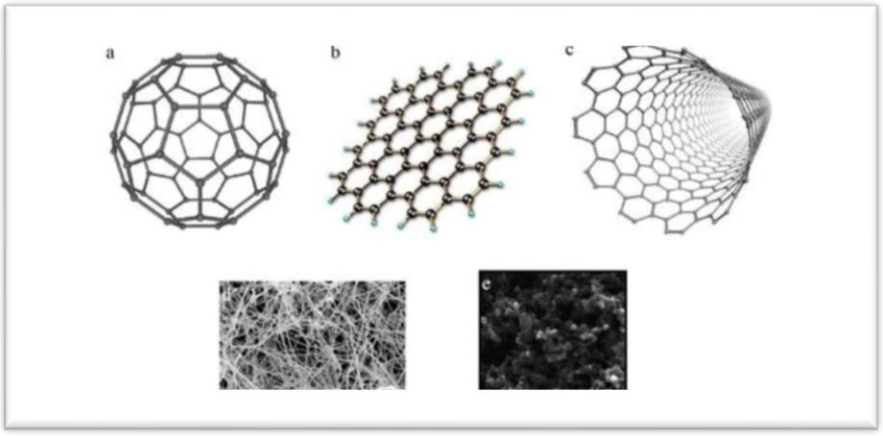
Inorganic nanoparticles are particles that are not made up of carbon. Metal and metal oxide based nanoparticles are generally categorised as inorganic nanoparticles.

a)Metal based Nanoparticles that are synthesised from metals to nanometric sizes either by destructive or constructive methods are metal based nanoparticles. Almost all the metals can be synthesised into their nanoparticles. The commonly used metals for nanoparticle synthesis are

aluminium (Al), cadmium (Cd), cobalt (Co), copper (Cu), gold (Au), iron (Fe), lead (Pb), silver (Ag) and zinc (Zn). The nanoparticles have distinctive properties such sizes as low as 10 to 100nm, surface haracteristics like high surface area to volume ratio, pore size, surface charge and surface charge density, crystalline and amorphous structures, shapes like spherical and cylindrical and colour, reactivity and sensitivity to environmental factors such as air, moisture, heat and sunlight etc.

b) **Metal oxides based**. The metal oxide based nanoparticles are synthesised to modify the properties of their respective metal based nanoparticles, for example nanoparticles of iron (Fe) instantly oxidises to iron oxide (Fe_2O_3) in the presence of oxygen at room temperature that increases its reactivity compared to iron nanoparticles. Metal oxide nanoparticles are synthesised mainly due to their increased reactivity and efficiency The commonly synthesised are Aluminium oxide (Al_2O_3), Cerium oxide (CeO_2), Iron oxide (Fe_2O_3), Magnetite (Fe_3O_4), Silicon dioxide (SiO_2), Titanium oxide (TiO_2), Zinc oxide (ZnO). These nanoparticles have possess an exceptional properties when compared to their metal counterparts.

Carbon based The nanoparticles made completely of carbon are knows as carbon based . They can be classified into fullerenes, graphene, carbon nano tubes (CNT), carbon nanofibers and carbon black and sometimes activated carbon in nano size and are presented in Figure.20

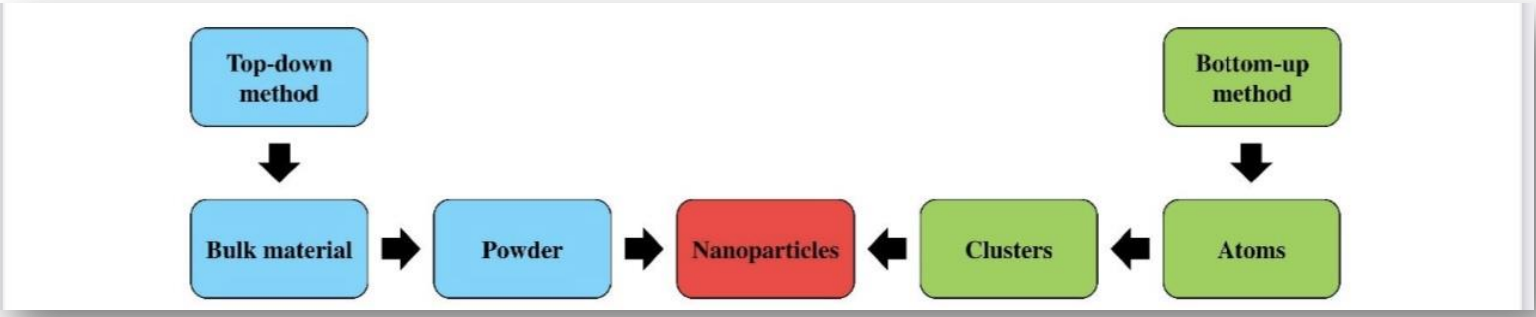


Carbon based nanoparticles: a – fullerenes, b – graphene, c – carbon nanotubes,

d – carbon nanofibers and e – carbon black

Synthesis of Nanoparticles

The nanoparticles are synthesised by various methods that are categorised into bottom-up or top-down method. A simplified representation of the process is presented in Figure



Bottom-up method

Bottom-up or constructive method is the build-up of material from atom to clusters to nanoparticles. Sol-gel, spinning, chemical vapour deposition (CVD), pyrolysis and biosynthesis are the most commonly used bottom-up methods for nanoparticle production.

a) **Sol-gel.**The sol – a colloidal solution of solids suspended in a liquid phase. The gel – a solid macromolecule submerged in a solvent. Sol-

gel is the most preferred bottom-up method due to its simplicity and as most of the nanoparticles can be synthesised from this method. It is a wet-chemical process containing a chemical solution acting as a precursor for an integrated system of discrete particles. Metal oxides and chlorides are the typically used precursors in sol-gel process . The precursor is then dispersed in a host liquid either by shaking, stirring or sonication and the resultant system contains a liquid and a solid phase. A phase separation is carried out to recover the nanoparticles by various methods such as sedimentation, filtration and centrifugation and the moisture is further removed by drying .

b) **Spinning**. The synthesis of nanoparticles by spinning is carried out by a spinning disc reactor (SDR). It contains a rotating disc inside a chamber/reactor where the physical parameters such as temperature can be controlled. The reactor is generally filled with nitrogen or other inert gases to remove oxygen inside and avoid chemical reactions . The disc is rotated at different speed where the liquid i.e. precursor and water is pumped in. The spinning causes the atoms or molecules to fuse together and is precipitated, collected and dried . The various operating parameters such as the liquid flow rate, disc rotation speed, liquid/precursor ratio, location of feed, disc surface, etc. determines the characteristics nanoparticles synthesised from SDR.

c) **Chemical Vapour Deposition (CVD**). Chemical vapour deposition is the deposition of a thin film of gaseous reactants onto a substrate. The deposition is carried out in a reaction chamber at ambient temperature by combining gas molecules. A chemical reaction occurs when a heated substrate comes in contact with the combined gas . This reaction produces a thin film of product on the substrate surface that is recovered and used. Substrate temperature is the influencing factor in CVD. The advantages of CVD are highly pure, uniform, hard and strong nanoparticles. The disadvantages of CVD are the requirement of special equipment and the gaseous by-products are highly toxic .

d) **Pyrolysis**. Pyrolysis is the most commonly used process in industries for largescale production of nanoparticle. It involves burning a precursor with flame. The precursor is either liquid or vapour that is fed into the furnace at high pressure through a small hole where it burn [13]. The combustion or by-product gases is then air classified to

recover the nanoparticles. Some of the furnaces use laser and plasma instead of flame to produce high temperature for easy evaporation . The advantages of pyrolysis are simple, efficient, cost effective and continuous process with high yield.

e) **Biosynthesis**. Biosynthesis is a green and environmental friendly approach for the synthesis of nanoparticles that are nontoxic and biodegradable . Biosynthesis uses bacteria, plant extracts, fungi, etc. along with the precursors to produce nanoparticle instead of convention chemicals for bioreduction and capping purposes. The biosynthesised nanoparticles has unique and enhanced properties that finds its way in biomedical applications 20

Top-down method

Top-down or destructive method is the reduction of a bulk material to nanometric scale particles. Mechanical milling, nanolithography, laser ablation, sputtering and thermal decomposition are some of the most widely used nanoparticle synthesis methods.

a) **Mechanical milling**. Among the various top-down methods, mechanical milling is the most extensively used to produce various nanoparticles. The mechanical milling is used for milling and post annealing of nanoparticles during synthesis where different elements are milled in an inert atmosphere [16]. The influencing factors in mechanical milling is plastic deformation that leads to particle shape, fracture leads to decrease in particle size and cold-welding leads to increase in particle size .

b) **Nanolithography**. Nanolithography is the study of fabricating nanometric scale structures with a minimum of one dimension in the size range of 1 to 100 nm. There are various nanolithographic processes for instance optical, electron-beam, multiphoton, nanoimprint and scanning probe lithography . Generally lithography is the process of printing a required shape or structure on a light sensitive material that selectively removes a portion of material to create the desired shape and structure. The main advantages of nanolithography is to produce from a single nanoparticle to a cluster

with desired shape and size. The disadvantages are the requirement of complex equipment and the cost associated

c) **Laser ablation**. Laser Ablation Synthesis in Solution (LASiS) is a common method for nanoparticle production from various solvents. The irradiation of a metal submerged in a liquid solution by a laser beam condenses a plasma plume that produces nanoparticles . It is a reliable top-down method that provides an alternative solution to conventional chemical reduction of metals to synthesis metal based nanoparticles. As LASiS provides a stable synthesis of nanoparticles in organic solvents and water that does not require any stabilising agent or chemicals it is a 'green' process.

d) **Sputtering**. Sputtering is the deposition of nanoparticles on a surface by ejecting particles from it by colliding with ions . Sputtering is usually a deposition of thin layer of nanoparticles followed by annealing. The thickness of the layer, temperature and duration of annealing, substrate type, etc. determines the shape and size of the nanoparticles .

e) **Thermal decomposition**. Thermal decomposition is an endothermic chemical decomposition produced by heat that breaks the chemical bonds in the compound . The specific temperature at which an element chemically decomposes is the decomposition temperature. The nanoparticles are produced by decomposing the metal at specific temperatures undergoing a chemical reaction producing secondary products. Table 1 lists some of the nanoparticles synthesised from these methods.

Categories of the nanoparticles synthesised from the various methods20

Category	Method	Nanoparticles
Bottom-up	Sol-gel	Carbon, metal and metal oxide based
	Spinning	Organic polymers
	Chemical Vapour Deposition (CVD)	Carbon and metal based
	Pyrolysis	Carbon and metal oxide based
	Biosynthesis	Organic polymers and metal based
Top-down	Mechanical milling	Metal, oxide and polymer based
	Nanolithography	Metal based
	Laser ablation	Carbon based and metal oxide based
	Sputtering	Metal based
	Thermal decomposition	Carbon and metal oxide based

Zinc oxide

zinc oxide nanoparticle (ZnO NP) is a white odorless powder with a molecular weight of 81.38 g/mol. It is a wide band gap semiconductor (3.37 eV at room temperature) with a wurtzite crystal structure. ZnO NPs are used for both industrial and biomedical applications because of their unique electrical, optical, catalytic, and photochemical properties. These properties are easily tuned according to the requirements, by changing the size, doping with other compounds, or adjusting the synthesizing conditions. One of the most attractive features of the ZnO NPs is that nanostructures with unique morphologies such as nanohelix and nanorings can be synthesized easily and cost-effectively. A number of ZnO NPebased products are available in the market. ZnO NPs are used in cosmetics as UV-blocking agents. Apart from that, ZnO NPs are used in food packaging, ointments, and daily-care products because of their antimicrobial and antifungal properties.21

Synthesis methods of ZnO NPs

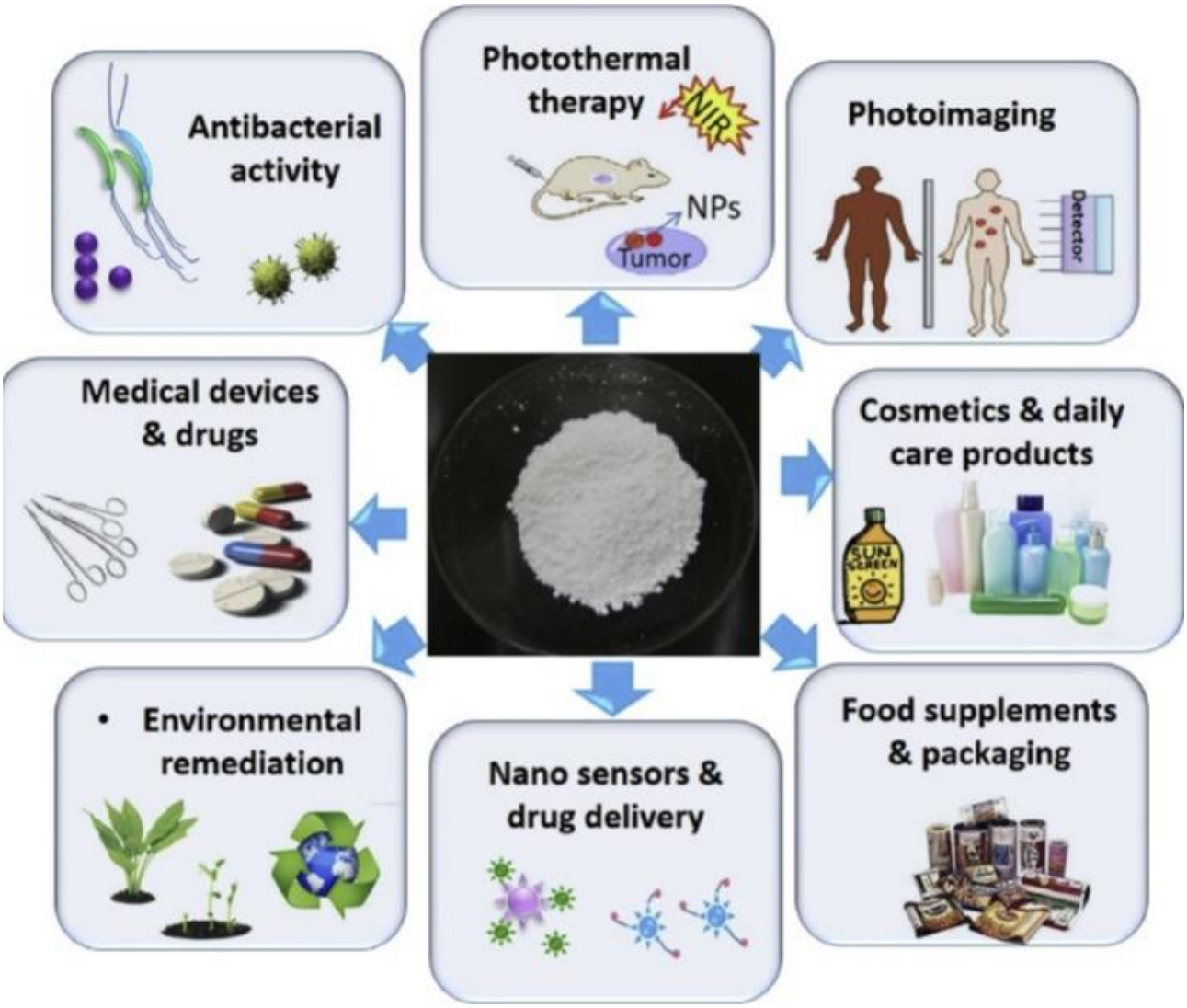
ZnO NP synthesis methods open up an array of possibilities for

synthesizing NPs with diverse morphology and size. The various

characteristics such as size, shape, and surface chemistry of ZnO NPs can be fine-tuned with various reaction parameters such as temperature, solvent, time, etc. Because the various characteristics such as size, shape, and surface chemistry influence the application and toxicity of ZnO NPs, it is vital to properly select the synthesis mode. The synthesis protocol needs to be selected based on the expected application. The major approaches for ZnO NP synthesis include physical methods, chemical methods, and biological methods. Physical methods include physical vapor deposition , thermal evaporation , etc. Chemical methods are the mainly used approaches, especially precipitation method, hydrothermal method , sol-gel method , and chemical vapor deposition technique . Biological methods of ZnO NP synthesis are relatively new, aimed at an eco-friendly method. Biological methods such as synthesis from plant extract help in avoiding toxic chemicals .21

Biomedical application of ZnO NPs

- Antibacterial agent
- Cancer therapy
- Bioimaging
- Drug delivery
- Gene delivery
- Biosensors
- Pharmaceutical and cosmetic applications
- Neurobiological application
- Electronic applications. 21



Preparation of ointments

The ointment base was prepared by mixing the hard paraffin (5 %), soft paraffin (90 %) and lanolin (5 %) by the fusion method. The ointments of bulk ZnO (20 %) and ZnO nanoparticles (2 %) were prepared in this ointment base Comparative evaluation for wound healing potentials of bulk and nano forms of zinc oxide ointment by the incorporation method.

The prepared ointment base, bulk ZnO ointment and ointment of ZnO nanoparticles were stored at 4 ◦C till further uses for wound healing studies.22