

## Current Innovations in Novel Drug Delivery Technologies for Herbal Medicine Administration: An Update

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### ABSTRACT

Herbal medications have attracted widespread interest from consumers and researchers in recent years because to its aesthetic value, increased patient comfort, and significant therapeutic results. Novel delivery methods for herbal medications have various advantages compared to conventional formulations. It comprises improving solubility, bioavailability, and toxicity protection, among other things. By combining herbal pharmaceuticals into appropriate dose forms, they may be administered in a more upright manner with increased efficacy. This can be accomplished by developing innovative drug delivery mechanisms for such medications. Polymeric nanoparticles, nanocapsules, phytosomes, emulsions, microspheres, and other systems are examples of such systems.

### INTRODUCTION

Herbal medications have gained worldwide interest due to their aesthetic value, increased patient compliance, and significant therapeutic results. Ethnobotanical knowledge on such plants and their use by indigenous cultures is valuable in the preservation of traditional medical systems, ecology, and the growth of health care systems [2-3]. There are numerous varieties of plants accessible all over the world. such plant including Aloe vera, neem, Murraya, Carica jimenezii, garlic, and other plants are examples [4-5].

Novel drug delivery strategies for herbal medications have various advantages compared to conventional formulations [6]. The optimal dosage of the particular drug is delivered to the patient in such a way that it reaches the specific site of action' and produces therapeutic benefits [7]. Certain medications have an optimal concentration range within which they provide the most benefit, while levels above or below this range might be harmful or provide no therapeutic effect at all.

Herbal remedies are known to be rich suppliers of phytochemical components, which are

important in the creation of novel medications. For thousands of years, people have used herbal medicine without scientific understanding or appropriate instructions. Each component of a plant, including the roots, stems, leaves, flowers, fruits, and seeds, has been scientifically proven to have medicinal characteristics. Yet, it has been observed that certain plants are poisonous and have negative effects on the body and should not be consumed (Wink, 2010). To produce a medication from phytochemicals, the bioactive extract should be standardised based on the active compound and subjected to restricted safety trials. There has been a rise of interest in rediscovering medicinal herbs as a supplier of possible medication candidates in recent years. As a result, the goal of this review is to grasp the knowledge and present condition of medicinal plants in order to transform them into a future source of herbal pharmaceuticals.

Ayurveda is herbal system that has been practised primarily in India for over 5,000 years. It emphasises the importance of the body, mind, and spirit in disease prevention and treatment while also including herbal remedies. Volume 82 of the IARC Monographs. Ayurveda is evidence of the extensive history of plant medication in India. Atharvaveda, which dates back to approximately 1500–1000 BC and is a Sanskrit word that means "knowledge of life," gave rise to Ayurveda. The two most well-known Ayurvedic treatises are Charak Samhita and Sushruta Samhita, but many more have been written throughout the years, including Kashyap Samhita, Agnivesh Tantra, Bela Samhita (600), and Madhava Nidan. Indian Materia Medica, which made great use of leaves and bark, flowers, fruits, roots, tubers, and fluids, was predominately composed of vegetable materials. The base of Ayurveda pharmacology was the philosophy of rasa, vipaka, virya, and prabhava, which did not clearly of both a medicine and a diet and drug because both were essential components of therapy. 700 herbal medicines were detailed by Charak, Sushruta, and Vagbhata along with their therapeutic effects. Based on clinical

results, 50 different drug categories have been identified, including digestive stimulants, laxatives, anti-diarrhea, anti-hemorrhoids, anti-inflammatory, anti-pruritic, anti-asthmatic, antiepileptic, anti-helminthic, haemoptetic. India has a rich of documented and well-utilized traditional herbal medical knowledge.

The following are the fundamental requirements for entry into developed countries include:

1. Well-documented traditional use.
2. Single-plant remedies.
3. Medicinal plants free of heavy metals or pesticides, etc.
4. Calibration using the activity and chemical profiles.
5. Safety and stability

#### CONVENTIONAL DOSAGE FORMS

Several drug delivery and drug targeting systems are now being developed to reduce deterioration and disappearance of drugs, eliminate unwanted side effects, and maximize drug bioavailability and the percentage of the medication accumulated in the necessary zone. A novel medication delivery system is a new method to drug administration. It allows the medicine to function for a longer period of time and more effectively.

To overcome the limitations of conventional medication delivery systems [8].

The limits of conventional dose formulations are as follows [9].

- 1) Poor patient compliance, higher chance of skipping a dosage of a medicine with a short half-life that requires frequent administration.
- 2) Unavoidable variations in drug concentration may result in under or overmedication.

3) The average peak-valley plasma concentration period profile is established, making steady-state conditions challenging to achieve.

4) Changes in drug levels may precipitate undesirable consequences, particularly in the case of a medicine with a low therapeutic index, when overmedication occurs.

#### NDDS

Control of drug distribution is achieved in NDDS technology by introducing the drug in a carrier system or by altering the chemical's arrangement at the molecular level. The following benefits are associated with novel drug delivery methods [10].

1. Improvement in solubility.
2. Enhanced bioavailability.
3. Protection from toxicity.
4. Pharmacological action is increased.
5. Stability enhancement.
6. Better dispersion of tissue macrophages.
7. Consistent delivery.
8. Protection against physical and chemical deterioration.

#### HERBAL DRUG

Herbs or An herbal formulation is a medication dose type that includes one or more processing plants precise sufficient to offer certain dietary, cosmetic, and/or other benefits intended for use in treating, preventing, or curing human or animal diseases, as well as to change the anatomy or physiology of people or animals.

Preparations are made by undergoing extraction, distillation, expression, fractionation, purification, concentration, or fermentation operations on entire plants, fragmented or chopped plants, or plant components. Crushed herbs compounds, tinctures, extracts, essential oils, expressed juices, and processed exudates are examples of these [11-12].



Fig.no.1 Advantages of Herbal Drugs

### LIMITATIONS OF HERBAL DRUGS

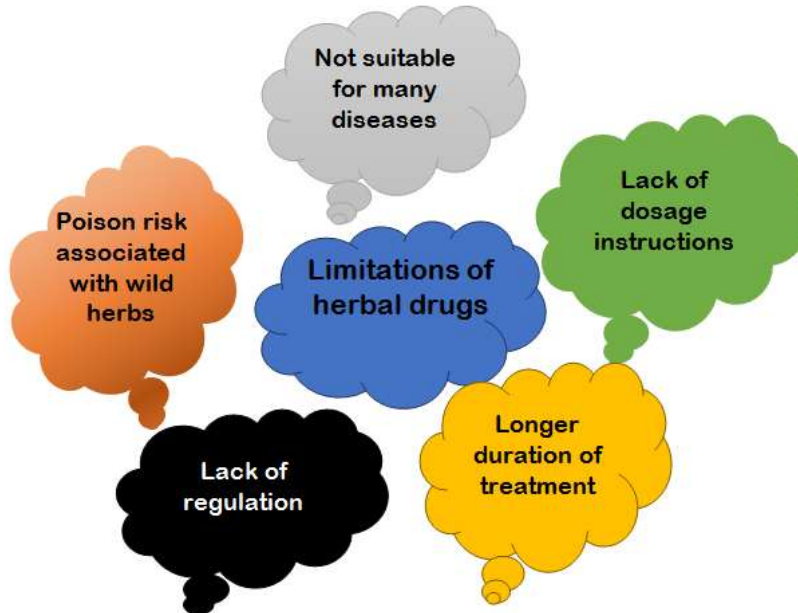


Fig no.2 Limitation of herbal drug

Herbs or The use of herbal medicines to treat a range of disorders with less hazardous side effects and greater therapeutic results is growing in popularity in the modern world. The excessively acidic pH of the stomach has a significant likelihood of destroying several components in herbal medications. The liver may metabolize other

drugs before they enter the blood. The actual dosage of the drug will not reach into the blood. As a result , the exact amount of drugs may not enter the bloodstream. There will be no therapeutic effect if the drug does not enter the blood at a certain level defined as the 'minimum effective level' [13].

### TYPES OF NOVEL HERBAL DRUG DELIVERY SYSTEMS

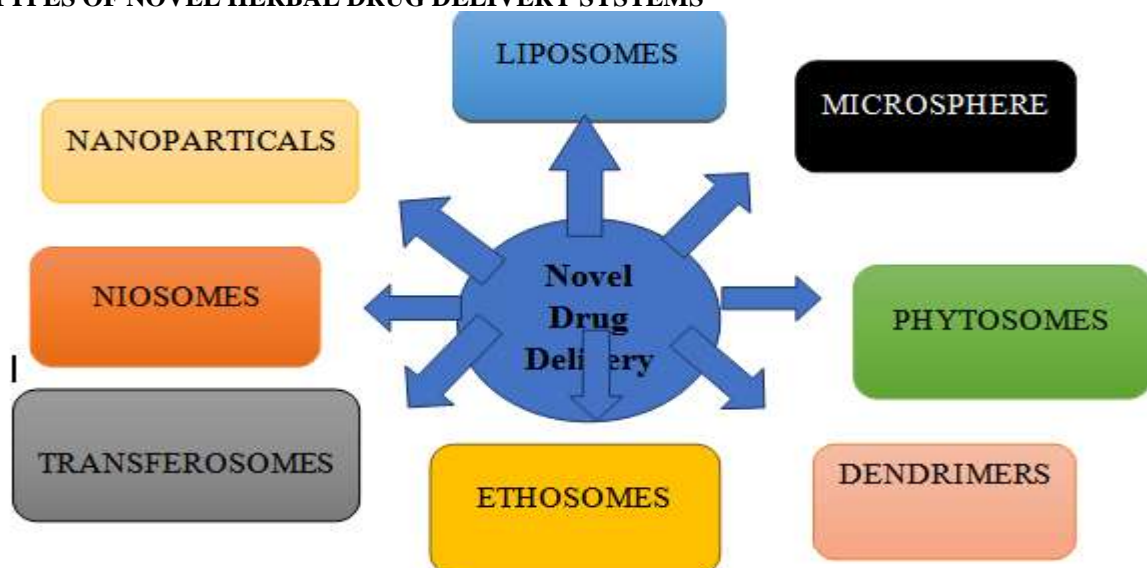

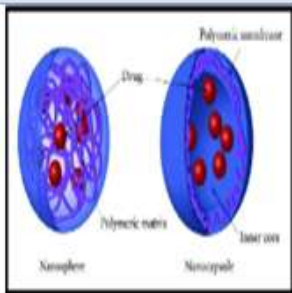
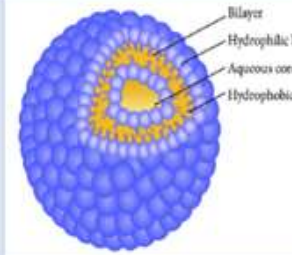


Fig no.3 Novel drug delivery

NDDS	Description	Methods of preparation	Advantages	structure
<b>Liposomes</b>	Liposomes are basically vesicles or "bags" in which an aqueous volume is completely surrounded by a membrane comprised of lipid (fat) molecules, often phospholipids.	1)Drying down lipids from organic solvent. 2)Dispersing the lipid in aqueous media. 3) Purifying the resultant liposome. 4) Analyzing the final product	1)the high biocompatibility 2)the easiness of preparation 3) effectively as the chemical versatility that permits the loading of hydrophilic, amphiphilic, and lipophilic substance [14]. 4)Sustained and controlled release of formulation can be possible	 <p>Liposome for Drug Delivery</p>
<b>Nanoparticles</b>	Nanoparticles are solid, colloidal, particles ranging 10-1000nm in which active ingredient dissolved/entrapped/encapsulated	1)Solvent evaporation 2)Nanoprecipitation 3)Emulsification/solvent diffusion 4) Salting out 5) Dialysis 6)Supercritical fluid technology (SCF) [15]	1)delivered directly to the site of action by the nanoparticulate technology. 2)Drug solubility and pharmacokinetics can enhance by encapsulating drugs within nanoparticles.	
<b>Niosomes</b>	Niosomes basically consist of non ionic surfactant which provide benefit over phospholipid so they are more affordable & economical. [16].	1) Ether Injection Method 2)Hand Shaking Method 3)Sonication Method 4)Reverse Phase Evaporation Method	1)High patient compliance compare to oily dosage form as the vesical suspension is water based vehical. 2)They improve oral bioavailability of poorly absorbed drug & enhance skin penetration of drug. [17].	


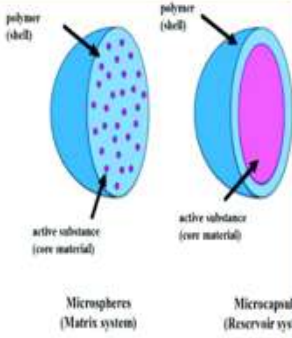
<p><b>Proniosomes</b></p>	<p>Proniosome gel system is an improvement over niosome and may be used in a variety of ways to deliver actives to the target place. Proniosomal gels are the formulations that become niosomes when in situ hydrated with skin water. Proniosomes are hydratable, water-soluble carrier particles with a surfactant coating [17].</p>	<p>-</p>	<p>1)stable during storage and sterilization.          2) Easy to transfer and distribution</p>	<p>-</p>
<p><b>Ethosomes</b></p>	<p>Ethosomes are a minimally modified version of the well-known drug carrier liposome.</p>	<p>1)cold method          2)Hot method</p>	<p>1)Low risk profile- The technology has no large-scale drug development risk since the toxicological profiles of the ethosomal components are well documented in the scientific literature.          2)Ethosomes are a delivery system for a broad range of medications (peptides).</p>	
<p><b>Microsphere</b></p>	<p>Microsphere are flowable powder consisting of protein or synthetic polymer which are biodegradable in nature &amp; ideally having partial size less than 200 µm</p>	<p>1)Spray Drying          2) Solvent Evaporation          3) Single emulsion technique          4) Double emulsion technique          5)Solvent extraction          6)Quasi emulsion solvent diffusion [18].</p>	<p>1)Improve flow of powder          2)production of SR CR &amp; targeted medication</p>	

Table no.1

**Phytosomes**

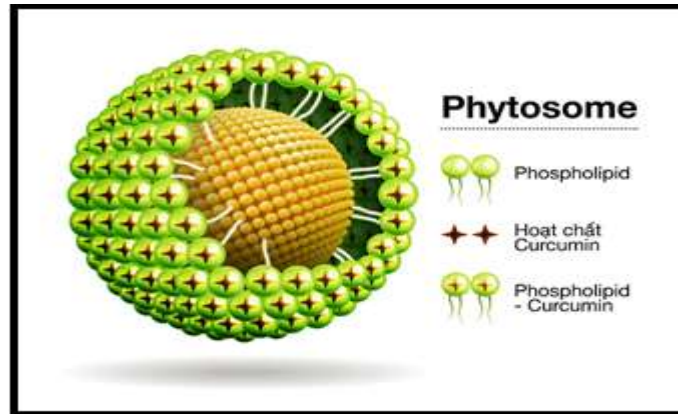
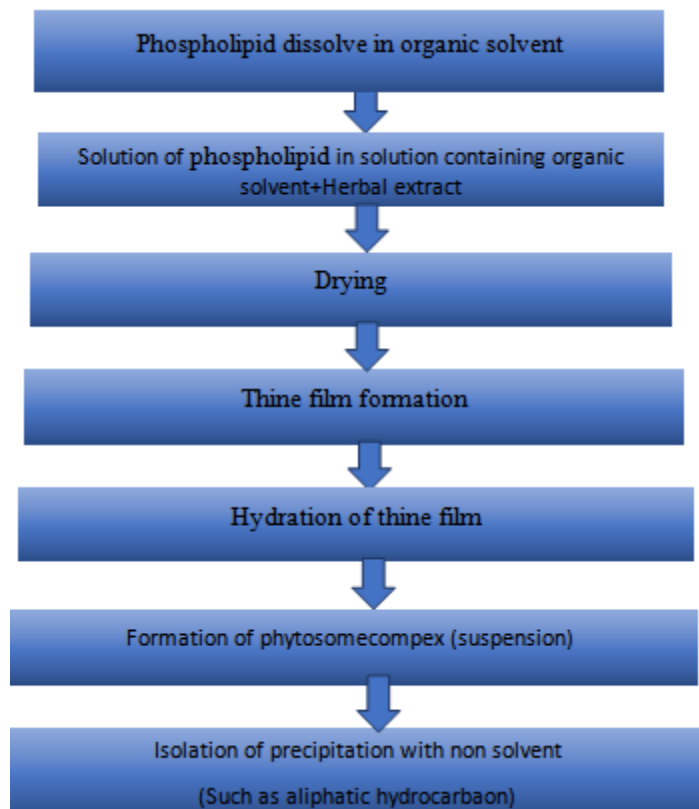


Fig no.4 structure of phytosome

Most of the bioactive constituents of phytomedicines are flavonoids, which are poorly bioavailable when taken orally. are more capable of

crossing lipid-rich biomembranes than basic herbal extracts, making them more accessible. [19]

**Method of preparation of phytosome**



**HERBAL MEDICINE**

World Health Organization recently described plant medication as therapeutic techniques that existed for thousand years before the invention and spread of modern medicine both

are still in use.Traditional medicine is the synthesis of generations of indigenous medical practitioners' therapeutic expertise.

Medicines or herb used for various purpose like netraceuticals which prevent disease or

optimum nutrition, cosmaceuticals which includes use of herbs in cosmetics as they give better effect and least side effect. and biopesticides which are biologically or herbs used widely as having no side

effect or toxic effect on consumers health. a brief introduction about nutraceuticals, cosmaceutical and pesticides given below including classification herbs and marketed preparation

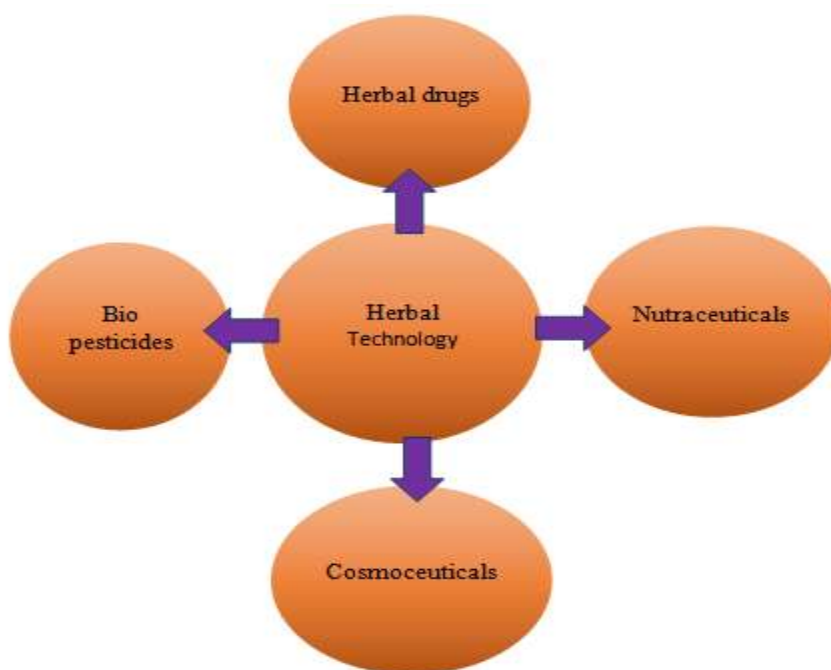


Fig no.5 Herbal technology

Nutraceuticals on the market today consist of both foods and non-traditional foods.

•Classic nutraceuticals are essentially entire meals that are naturally occurring; they provide fresh

knowledge about their potential health qualities. Apart than how they are perceived by consumers, the foods themselves have not changed. Lycopene in tomatoes and omega

Sr.No	Chemical constituent	source	Potential benefit
I)	Carotenoids(Isoprenoids)	Tomatoes, grapefruit, guava, papaya	Antioxidant activity, protects against formation of cancer
1)	Lycopene	watermelon	Mainly bladder, cervical
2)	Lutin	Corn, egg, spinach	Anticancer activity (colon), cataracts, protects the eyes Against development of age related muscular degeneration.
3)	Carotene	Carrots, various fruits and vegetables Carrots Oranges, Corn, avocado	Antioxidant activity which neutralizes free radicals, protect cornea against UV light. Antioxidants, anticancer
II)	Dietary fibre		
	Soluble fibre	Legumes, oats, barely, some fruits	Anticancer, helpful in maintaining the digestive tract
	Insoluble fibre	Whole grain	Anticancer(colon), helpful in

		foods Wheat and corn bran, nuts	maintaining the digestive tract
III)	Probiotics/Prebiotics	Yogurt, other dairy and non dairy Applications	Improves gut health and overall immunity
IV)	Omega 3 Fatty Acids	Salmon, Flax seed	Potent controllers of the inflammatory processes, Maintenance of brain function, Reduce cholesterol disposition
V)	Antioxidants		
	Flavonones	Citrus fruits	Antioxidants, Anti cancer
	Flavones	Fruits, Vegetables, Soyabean	Antioxidants, Anti cancer
	Flavonols	Onions, apples, tea, broccoli	Antioxidants

Table no.2

•Non-Traditional Nutraceuticals are foods that have been bred for agriculture or have additional nutrients, to boost their nutritional values. Examples include  $\beta$  carotene-enriched rice, and

soybeans, orange juice fortified with calcium, cereals with added vitamins or minerals (Rajat et al., 2012).

**Classification of nutraceuticals**

Sr.No	Marketed Nutraceutical	Category	Ingrident	manufacturer
1	Proteinex®	Protein supplement	Predigested proteins, vitamins	Pfizer Ltd., Mumbai, India
2	Calcirol D-3®	Calcium supplement	Calcium and vitamins	Cadilla healthcare limited, Ahmedabad, India
3	Threptin® Diskettes	Protein supplements	Proteins and vitamin B	Raptakos, Brett & Co. Ltd., Mumbai, India
4	Beneflora® probiotic	Maintain gastrointestinal health	Lactobacillus acidophilus, bifidobacterium bifidum	Nupro, USA
5	Ferradol Food® Powder	Nutrition supplement	Carbohydrates, proteins, Niacinamide, calcium, iron, zinc, vitamins	Pfizer Limited, India
6	Revital®	Daily health supplement	Ginseng, vitamins and minerals	Ranbaxy
7	Glowelle®	Beauty drink	antioxidants, vitamins and	Nestlé



			botanical and fruit extracts	
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Table no.3



Fig no.6 Marketed product of Nutraceutical

Survey released today, the Indian nutraceutical market, which had a 2011 valuation of \$ 1,480 million, might reach \$ 2,731 million in 2016. Functional foods will have the fastest growth through 2015, followed by dietary supplements, predicts corporate research and consultancy company Frost & Sullivan. Nonetheless, the biggest market for nutraceutical makers will be dietary supplements, particularly herbal and dietetic supplements.

The food products used as nutraceutical are categorized as:

1. Probiotic
2. Prebiotic
3. Dietary fiber
4. Omega 3 fatty acid Antioxidant

### 1. Probiotic

Probiotic are "good" bacteria that prevent the formation of dangerous bacteria and maintain the health of your digestive tract.

The term "probiotics," which means to "for life," refers to living microorganisms that, when taken in sufficient quantities, benefit the host's health. They are beneficial bacteria that encourage nutritious food absorption and good digestion.

### 2. Prebiotic

Prebiotic are carbohydrates that the body is unable to process. They serve as probiotics' meal. Prebiotics are dietary components that support a certain type of gut microbes by primarily consisting of nonstarch polysaccharides and oligosaccharides

that are poorly digested by human enzymes. They encourage the growth of good bacteria rather than bad. Typical prebiotics include: Oligofructose. Breast milk oligosaccharides, inulin, galacto-oligosaccharides, and lactulose. Natural sources of the prebiotic oligofructose include wheat, onions, bananas, honey, garlic, and leeks. Oligofructose can also be produced enzymatically from sucrose or isolated from chicory root.

### 3. Dietary fiber

Dietary fiber, often as roughage, is the known indigestible part of plant-based diet. It is made up of two major parts:

Soluble fibre is easily fermented in the colon into gases and physiologically active byproducts, and it can be prebiotic and viscous.

Insoluble fibre, not dissolve in water, is metabolically inactive and provides bulking, whereas prebiotic fibre ferments in the large intestine. Bulking fibres absorb water as traverse the intestinal tract, making defecation easier.

### 4. Omega-3 fatty acids

Omega-3 fatty acids are polyunsaturated fatty acids (PUFAs) having a double bond (C=C) at the third carbon atom from the carbon chain's terminus. The fatty acids have two ends: the carboxylic acid (-COOH) end, which is regarded the chain's beginning, so "alpha," and the methyl (CH<sub>3</sub>) end, which is called the chain's "tail," therefore "omega."

Walnuts, flaxseed oil, echium oil, and hemp oil are common plant sources of the omega-3 ALA fatty acid, whereas sources of the animal

omega-3 EPA and DHA fatty acids include fish oils, egg oils, squid oils, and krill oil.

### 5. Antioxidants

Antioxidants are compounds that could guard against the harm that unstable molecules called free radicals do to cells.

Free radicals interact and are stabilised by antioxidants, which may limit some of the harm they may otherwise do. Cancer may result from free radical damage. Beta-carotene, lycopene, vitamins C, E, and A, among other chemicals, are examples of antioxidants. A substance that may slow down or stop the oxidation of other molecules is an antioxidant.

The chemical process of oxidation involves the exchange of electrons from a molecule to an oxidising agent.

### 6. Cosmeceuticals

Cosmeceuticals The study of altering appearance is known as cosmetology. (2014) Saraf et al.

Cosmetics with biologically active chemicals that claim to provide therapeutic or drug-like effects are known as cosmeceuticals.

Herbal cosmetics, often known as products, are prepared using a variety of cosmetic chemicals that are legal to use as a basis before adding many herbal elements to exclusively give certain cosmetic advantages.

Herbal cosmetics are currently popular in the fashion and beauty industries. Since natural products provide the body with nutrients, improve health, and give satisfaction because they are free from synthetic chemicals and have comparatively fewer side effects than synthetic cosmetics.

Classification of Cosmeceuticals				
Retinoid	Sunscreens	Moisturizers	Depigmentation	Proteins/peptides

Table no.4

### Herb used in cosmetics

Sr.No	Chemical constituent	Source	Potential benefit
1	Glycyrrhizin Glycyrrhithinic acid	Glycyrrhizin Glycyrrhithinic acid	Reduces skin discolorations and Anti-inflammatory
2	Safranal, Carotenoid	Saffron	Post bath massage
3	Flavonoids Triterpenoids	Lemon	Whitening, astringent depigmentation
4	Sesquiterpenes, Sesquiterpenols	Sandal wood	Skin lotion

Table no. 5

**Marketed preparations**

Sr. No.	Product	Brand name	company
1	Face Wash	Deep Cleansing Apricot Face Wash	Himalaya herbals
2	Cream	Herbal massage cream	Ayur Herbals
3	Hair oil	Amla Brahmi hair oil	Ayur Herbals
4	Anti-Ageing cream	Dabur Uveda Age Renew 5 cream	Dabur

**Table no.6**

**Marketed product for cosmeceuticals:**



**Fig no.7** Marketed product for cosmeceuticals

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