

E-ISSN: 2321-2187 P-ISSN: 2394-0514 www.florajournal.com IJHM 2024; 12(1): 34-43 Received: 28-10-2023 Accepted: 10-12-2023

Mahendra Jain

Technocrats Institute of Technology-Pharmacy, Anand Nagar, BHEL, Opposite Hathaikheda Dam, Bhopal, Madhya Pradesh, India

Kinjal Parikh

Faculty of Pharmacy, The Maharaja Sayajirao University of Baroda, Kalabhavan, Vadodara, Gujarat, India

Ganesh Shevalkar

Department of Pharmaceutics, Sandip Institute of Pharmaceutical Sciences, Mahiravani, Nashik, Maharashtra, India

Parth Thakkar

Faculty of Pharmacy, The Maharaja Sayajirao University of Baroda, Kalabhavan, Vadodara, Gujarat, India

Rakhee Kapadia

SIRT-Pharmacy, SAGE University, Sahara Bypass Road, Katara Hills, Extension, Bhopal, Madhya Pradesh, India

Corresponding Author: Rakhee Kapadia SIRT-Pharmacy, SAGE University, Sahara Bypass Road, Katara Hills, Extension, Bhopal, Madhya Pradesh, India

International Journal of Herbal Medicine Available online at www.florajournal.com



Introduction to functional performance of bio-based emulsifiers, natural preservatives, lipids, and natural surfactants

Mahendra Jain, Kinjal Parikh, Ganesh Shevalkar, Parth Thakkar and Rakhee Kapadia

DOI: https://doi.org/10.22271/flora.2024.v12.i1a.918

Abstract

Bio-based products can be obtained from natural renewable resources or produced after suitable bioprocessing. Almost every industry/sector, including energy, nutraceuticals, packaging, plastics, and many more, is currently concentrating on making bio-based materials, as these materials are bio-renewable, degradable, and environmentally safe. Bio-based nutraceuticals have gained popularity in recent decades due to their beneficial effects on the population and their role in lowering the risk of different diseases. In the present review, we have focused on the functional performance of various bio-based emulsifiers, natural preservatives, lipids, and surfactants with in-depth detail on their classification, functional roles, microorganisms involved in their production, and future perspectives. Thus, for commercial production, the use of renewable resources over fossil-based resources can provide tremendous advantages like protection to the environment, decreased production cost, and compounds with equal or improved yield.

Keywords: Bio-based emulsifiers, natural preservatives, lipids, natural surfactant

Introduction

Bio-based products are obtained from biomass (any organic, non-fossil-derived living matter which is renewable) after the suitable physical, chemical, or biological processing. Biomass generally includes crops, waste material (obtained from crops, wood, animals, or industries), and microorganisms (bacteria and fungi)^[1]. This concept has primarily emerged to decrease the use of fossil-based products to increase resource efficiency by using natural renewable resources. The bio-based materials can be used as such or are processed in several steps to form bio-synthetic materials from bio-based feedstock (crops, waste material, and microorganisms) ^[2]. These products are entirely or partially derived from the bio-based feedstock or biomass processed either by physical, biological (microorganism/biotechnology modified enzymes or microorganisms), or chemical methods (biochemical/thermochemical)^[3]. Generally, not all bio-based products are biodegradable and vice versa. Bio-based materials are the greener alternatives to petroleum-based materials. Large-scale production can act as a carbon sink because of low carbon emissions and are renewable/ recurring ^[4-5]. Apart from being the greener alternative, several environmental factors related to land, air, and water should be considered thoroughly ^[6]. Notably, one should consider the ecological imbalance that can arise by continuously extracting the nutrients from plant resources and maintaining soil health by replenishing the necessary nutrients ^[1]. Generally, bio-based nutraceuticals / ingredients are extracted directly from biomass (crops) or produced by microorganisms (bacteria and algae). In some industries, bio-based nutraceuticals are produced as a co-product, while most of the feedstock is consumed for producing biofuels and chemicals, which ultimately reduces the overall cost of products ^[7]. Also, a broad category of natural compounds can act as nutraceuticals like lipids, vitamins, minerals, surfactants, preservatives, probiotics, etc. This review focuses mainly on the functional performance of bio-based lipids, surfactants, preservatives, and emulsifiers in biological processes.

Biosurfactants/ Bio emulsifiers

Surfactants are amphiphilic compounds having hydrophilic as well as hydrophobic parts. It could be synthetic or natural. Synthetic surfactants are produced by chemical synthesis, whereas natural surfactants are produced mainly by microorganisms.

Synthetic surfactants are widely used in various sectors; however, they harm the environment ^[8]. Besides this, the synthetic surfactants also have adverse effects on the human body, like changing membrane permeability due to disrupting membrane integrity, ulcer formation, skin and eye irritation, and excessive mucous production ^[9-10]. Concerning this, the need for eco-friendly, readily producible, and biodegradable surfactants is intensifying. Here the surfactants which are obtained from microorganisms have come into focus. These surfactants are also known as bio-based surfactants or biosurfactants ^[11].

Biosurfactants have industrial attention due to their versatility, producibility through fermentation, and ecofriendly nature. Besides this, low toxicity, biodegradability, functioning under severe pH and temperature regimes, generation from a renewable source, and stability are additional benefits of biosurfactants. The properties like reducing surface/ interfacial tension enable them to form emulsion and solution ^[12-13]. They also promote the absorption of biologically active compounds through physiological membranes ^[14, 15]. Microorganisms typically used for biosurfactant synthesis include bacteria, filamentous fungus, and yeast. These

microorganisms produce glycolipids, phospholipids, lipopeptides, fatty acids, saponins, and alkyl poly-glycosides. Recently, a European commission of standardization has derived a classification for biobased surfactants based on their biological content like wholly bio-based (>95% biological content), majority bio-based (50-94% biological content), and minority bio-based (5-49% biological content) ^[16]. Whereas, based on the primary and secondary metabolites present in their core structure, they are classified into four subclasses: i) glycolipid type, ii) fatty acid type, iii) lipopeptide type, iv) polymer type.

Bacterial biosurfactants are of particular interest because of their antibacterial, antifungal, and antiviral activities ^[17]. Pathogenic bacterial species, such as *Pseudomonas* and *Bacillus*, are commonly used to manufacture biosurfactants; however, their strains need to be handled safely to avoid toxicological risk ^[12]. To avoid these known risks, literature has recently reported the use of yeast-like fungi, such as *Starmerella bombicola*, and non-pathogenic bacteria, such as *Candida bombicola* ^[18]. The various biomasses and microorganisms used in the production of biosurfactants are shown in Table 1.

Table 1: Resi	dues in product	tion of biosurf	actants by mic	roorganisms ^[19] .

Waste Products	Producing microorganisms	Type of Biosurfactant
When	Pseudomonas aeruginosa BS2	Rhamnolipid
Whey	Bacillus sp.	Lipopeptides
	Pseudomonas aeruginosa GS3	Rhamnolipid
Molasses	Bacillus sp.	Lipopeptides
	Starmerella bombicola NBRC 10243	Lipopeptides, Sophorolipids
Frying Oil	Pseudomonas aeruginosa 47T2 4	Rhamnolipid
Corn steen liquer	Aureobasidium thailandense	Glycolipid
Corn steep liquor	Candida lipolytica	Giycolipid
Refinery oil waste	Yeast	Glycolipid

Emulsifiers with ultra-low molecular weight (e.g., rhamnolipids, sophorolipids) and average molecular weight (e.g., lipopeptides and phospholipids) have excellent market potential as they have the ability to combat surface and interfacial tension ^[20-22]. Trehalolipids, cellobiose lipids, mannosyl-erythritol lipids, rhamnolipids (produced from *Pseudomonas*), and sophorolipids (SLs) (derived from *Candida* and related species) are the glycolipids of highest interest ^[23-25]. Glycolipids and rhamnolipids have antibacterial capabilities due to their permeabilization action, which affects the integrity of the bacterial plasma membrane. They can also make bacteria more vulnerable to antimicrobial drugs by preventing biofilm formation ^[26].

Yeast-produced sophorolipids have grabbed the industry's interest. The molecule comprises a disaccharide called sophorose, linked to a long chain of hydroxyl fatty chains via a glycosidic bond with hydrophobic properties that provide biocidal, cytotoxic, and pro-inflammatory properties. It also has potential applications in the food, cosmetics, and bioremediation industries ^[27]. Sophorolipidis capable of

forming amphotericin B-loaded niosomal formulations with distinct structural and physicochemical features, as well as the biofilm-breaking capability and activity ^[28].

Lipopeptides (LPs) are made up of lipid segments connected to a peptide chain and have been shown to exhibit biological characteristics such as antibacterial effects. Daptomycin and polymyxin B are the well-known LPs derived from microorganisms and used in drug delivery systems [29-30]. Surfactin (SUR), iturin, and fengicin are three more wellknown LPs with a wide range of uses. They clump together polarized interfaces, such as oil/water and air/water, and function as wetting agents on solid surfaces (water/ solid). The capacity of biosurfactants to lower surface tension by placing their amphiphilic portions in specific regions of the membrane or surface in between the phases underpins this dynamic process. The antibacterial mechanism is thought to be the polymerization of LPs in cells to create transmembrane channels. The potential applications of biosurfactants are listed below in Table 2.

	Biosurfactants ^[31] .
--	----------------------------------

Type of Biosurfactant	Microorganism	Application	
Glycolipoproteins	Aspergillus niger	Antimicrobial activity	
Lichenisina	Bacillus licheniformis	Chelating agent and Hemolytic agent	
Lipopeptides	Bacillus subtilis	Biomedical application and antimicrobial	
Surfactin	Kurtzmanomyce ssp	Biomedical application	
Manosileritritol lipids	Candida antartica	Cell mediation and anti-inflammatory	
Conhonalinida	Candida bombicola	Emploifier	
Sophorolipids	Candida apicola	Emulsifier	

Glycolipids	Rhodococcus sp.	Bioremediation	
Gryconpids	Arthobacter sp.	Antimicrobial activity	
	Pseudomonas aeruginosa	Bioremediation	
Rhamnolipids	Pseudomonas putida	Dioremediation	
	Pseudomonas chlororaphis	Biocontrol agent	
	Renibacterium salmoninarum	Bioremediation	

Bio-Based Lipids

Lipids are a large group of organic compounds containing fatty acid chains. Broadly, lipids are classified as simple (fat, oil, and waxes), complex (phospholipids and glycolipids), and derived (fatty acids and econacids) lipids ^[32]. As mentioned earlier, biobased materials are obtained from living matter. Bio-based lipids can also be derived or extracted from biological sources like plants, animals, or oleaginous microorganisms ^[33]. The most widely used bio-based lipids in the nutraceutical industry are the derivatives of fatty acids (saturated and unsaturated), phytosterols, polar lipids (phospholipids and glycolipids), and certain oil-soluble vitamins due to their specific biological performance.

Functional performance of derivatives of fatty acids

Fatty acids are amphiphilic molecules containing a polar head and nonpolar tail. Depending on the presence of double bonds, they are classified as saturated (no double bonds inside chains) and unsaturated (have one or more double bonds) lipids ^[32]. Generally, unsaturated lipids are derived from plants. Oils obtained from the olive, peanuts, hazelnut, etc., are typical examples of unsaturated lipids ^[34]. These can further be classified as monounsaturated (MUFA) and polyunsaturated fatty acids (PUFA), depending on the number of double bonds in the side chain.

MUFA are reported to decrease blood LDL cholesterol levels and decrease the risk of cardiovascular diseases ^[35]. While PUFAs are further classified into two categories based on the position of the first double bond on the methyl terminal, i.e., the long-chain omega 3 and 6 series of PUFA contain 18 carbons in their chains. Both ω -3 and ω -6 fatty acids are obtained from plants and are derived from α -linoleic acid (ALA) and linoleic acid (LA), respectively ^[36]. They are also called essential fatty acids because they are precursors of other fatty acids, cannot be synthesized in the body, provide significant health benefits, and must be taken by diet /nutraceuticals. Studies have shown that essential fatty acids can reduce the risk of cardiovascular diseases, cancer, arthritis, type-2 diabetes, brain disorders, and neuropsychiatric disorders ^[37].

ω-6 fatty acids

Arachidonic acid (ARA), Υ -linoleic acid (GLA), and dihomo Υ -linoleic acid are members of the ω -6 fatty acid family. Few studies have shown that PUFA has a role in combating diabetes and its complications ^[38]. In diabetic neuropathy, the metabolism of linoleic acid to Υ -linoleic acid and other metabolites is disturbed, resulting in disturbed nerve flow and nerve conduction velocity. For a year, treatment and supplementation of linoleic acid have shown a synergistic effect on nerve blood flow and velocity ^[39]. Arachidonic acid and Υ -linoleic acid are also reported to reduce cholesterol levels and decrease cardiovascular mortality ^[40].

ω-3 fatty acids

(20:5. Eicosapentaenoic acid (EPA) n-3) and docosahexaenoic acid (DHA) (22:6, n-3) are the two most widely used nutraceuticals because of their functional roles in diseases several cardiovascular the treatment of (atherosclerotic coronary artery disease, and hypertriglyceridemia), central nervous system disorders (epilepsy, depression) and cancers (lung and prostate) [41-45]. EPA and DHA are prescribed in several conditions, including muscle damage [46].

Dietary ω -3 and ω -6 fatty acids are present in various nuts and vegetable oils, but microbial production is the most sorted out for commercial purposes because of its high ^[7-47]. For commercial purposes, high-quality ARA, GLA, DHA, and EPA can be obtained from microorganisms like bacteria, fungi, yeast, and microalgae ^[40]. Table 3 shows the name of microorganisms involved in the production of biobased ω -3 and ω -6 fatty acids.

Table 3: Microorganisms involved in the production of ω -3 and ω -6 fatty acids.

Sr. No.	Types of Fatty acids	Type of microorganism	Genus	Reference
1	GLA	Fungi	Genus Mucor, Mortierella, Rhizopus, Cunninghamella, and Zygorhynchus	[48]
2	ARA Fungi		Zygomycetes	[49]
2	АКА	Fungi	Oomycetes	[49]
3	ARA, EPA	Fungi	Mortierella alpine, M. alpine 20-17	[49,50]
4	EPA	Marine microalgae	Nannochloropsis species	[51]
5	EPA	Filamentous Fungi	Pythium ultimum, P. irregulare	
6	EPA	Marine bacteria	Shewanella sp., Synechococcus	
7	EPA	Yeast	Yarrowialipolytica, Recombinant Y. lipolytica	
8	DHA	Marine microalgae	Schizochytrium sp	
9	DHA	Marine microalgae	Crypthecodiniumcohnii	[57]

Phytosterols

Phytosterols are sterols present in plants. They comprise sterols (steroid alcohols) and stanols (saturated plant sterols) that are structurally similar to cholesterol except for a few variations in their structures ^[58]. To date, more than 250 species of the phytosterol family are identified, but the few common ones are sitosterol, stigmasterol, campesterol, brassicasterol, avenasterol, ergosterol, and spinosterol. They have only minor variations in their structures in either having a double bond at different positions in their triterpene ring structure or additional methyl/ethyl groups at C-24 side chains ^[59-60]. These structural variations in phytosterol molecules drastically differ their functional performances as compared to cholesterol molecules. The most prominent role of phytosterols is the cholesterol-lowering effect in humans. Multiple mechanisms can be attributable to the cholesterol-lowering effect. Few of them include competition between phytosterols and cholesterol for solubilization into bile salt

micelles; formation of poorly absorbable co-crystals of cholesterol and phytosterols in the gastrointestinal tract; reducing the quantity of free absorbable cholesterol by inhibiting the hydrolysis of cholesterol ester ^[61-62].

The European Commission, US FDA, and Canada too have approved the role of sterols and stanols in decreasing the risk of coronary heart disease ^[59]. Studies have shown that phytosterols in doses of 2-3 g daily effectively lower LDL, HDL, and TG levels by 10-15% ^[63-64]. Phytosterols can be obtained from dietary sources like vegetable oil, cereals, and a few fruits and vegetables in moderate quantities, but for hypocholesterolemic effect, the effective dose is higher, and hence few fortified foods in the form of salad dressings, margarine, and milk products have been developed. For commercial production of bio-based phytosterols, the microalgae of the genus *Dunaliella*are most widely used ^[7]. They act as a substrate for developing many steroidal drugs, antidiabetic, anti-inflammatory, chemoprotective, and wound healing properties ^[65].

Polar lipids

Another important category of lipid-based nutraceuticals consists of polar lipids. Polar lipids are amphiphilic molecules

containing a polar head and nonpolar tail, attributing them to emulsifying properties ^[66]. Two major classes of polar lipids fall under the category of phospholipids (glycerophospholipids) and sphingolipids (sphingomyelin and glycosphingolipids). Each one has a distinct functional role in the perceptional development of the brain ^[67].

Phospholipids and their functional role

Phospholipids are often termed glycerophospholipids and are the primary component of cell membranes. They control various cell membrane structural and functional properties, ultimately influencing the cell signaling pathways ^[68]. Structurally, phospholipids contain a polar head group composed of glycerol, alcohol, and phosphate group, and the two hydrophobic fatty acid chains are linked to glycerol at the C-1 position after esterification. Depending on the type of alcohol present in the polar head group, they are further phosphatidic classified as Acid (PA), phosphatidylethanolamine (PE), phosphatidylcholine (PC), phosphatidylglycerol (PG), phosphatidylserine (PS), and phosphatidylinositol (PI), and cardiolipin (CL) [69-70]. The details are listed in Table 4.

Table 4	4. Phos	nholinids	and thei	r functiona	l roles in	various	hiological	processes.
I abit	• •••••••••••••••••••••••••••••••••••	phonpius	and their	i functiona.	i ioics m	various	biological	processes.

Phospholipid Name	Alcohol of the polar head group	Functions	Reference
Phosphatidic Acid	c Acid - PA is converted to diacylglycerol by the lipid phosphate phosphohydrolases enzyme the metabolic precursor of many phospholipids.		[71]
Phosphatidyl- ethanolamine / cephalin	Ethanolamine	PE is abundantly present in the brain, including the white matter, nerves, and spinal cord. It is the major structural lipid of cell membranes.	[72]
Phosphatidylcholine /lecithin	Choline	They are the essential structural lipid of cell membranes and maintain the lipid bilayer structure.	[73]
Phosphatidylserine	Serine	They are most abundant in the brain and regulate various brain functions that diminish with age. They act as anchors for many proteins, including signal-transducing proteins. They are also involved in the cell-cell recognition and communication process.	[74]
phosphatidylinositol	Inositol	Constitute 10% of the total phospholipids of the brain. They are involved in cell signalling and regulation. PI is involved in DNA repair, transcription, and RNA dynamics.	[75]
Phosphatidylglycerol	Glycerol	Glycerol PG is the second most abundant lipid of lung surfactant, and lung maturity in babies depends on its concentration. It is also the precursor of CL.	
Cardiolipin	Phosphatidylglycerol	They are mainly present in the mitochondria and are involved in electron transport and oxidative phosphorylation processes. Its absence can result in various human metabolic disorders like Alzheimer's and Parkinson's disease.	

Glycerophospholipids are also the primary source of longchain PUFA in both the brain and central nervous system, and hence they are crucial for fetal brain development ^[77]. Besides that, literature shows phospholipids also provide intestinal immunity and protection against an infant's gastrointestinal infection ^[78]. In the elderly, they are reported to improve memory and reduce cholesterol absorption ^[79]. Few studies suggest dietary phospholipids can be effective in cancer, heart disease, and inflammations ^[80].

Sphingolipids and their functional performance

Structurally, members of the sphingolipid family contain a long chain (C-18) amino alcohol - sphingosine, in which the first three carbon atoms (forming the polar head) are analogous to glycerol of phospholipids and attached with a non-hydrolysable and non-variable long chain. The other fatty acid acyl chain is attached to the sphingosine molecule by a nitrogen ester (amide) linkage in sphingolipids. Sphingolipids are classified based on the group attached to the C-1 carbon atom, such as sphingomyelin and glycosphingolipids (ceramides), cerebrosides, and gangliosides ^[67]. Each one of them has a distinct functional role or performance inside humans. Sphingolipids are specifically present in the highest concentration in the brain and involved in brain development ^[81]. Studies have shown that their dietary supplementation will affect an infant's cognitive and neurobehavioral development ^[82].

Sphingomyelin

Structurally, sphingomyelin contains a phosphocholine group attached to the -OH group at the C-3 position. They are abundantly present in the myelin sheath of the central nervous system and play an essential role at grass root level right from the formation and integrity of the myelin sheath and maturation of axons and hence play a vital role in the cognitive development of the brain ^[83]. Variation in sphingomyelin metabolism can lead to severe mental diseases like Tay-Sachs disease, Niemann-pick disease, Gaucher disease, etc. ^[84]. Several research works suggest that they are helpful in inhibiting the carcinogenesis of the colon and preventing colorectal cancer ^[85, 86]. They also play an essential role in decreasing cholesterol absorption from the intestine and protecting the liver from cholesterol-induced steatosis ^[87].

Ceramides

The other important member of the sphingolipid family is ceramides containing a -OH group attached to the C-1 position and is the simplest of all. Functionally, it is a lipid mediator and is involved in various functions of the cell, including its death/ survival/ migration. They are also the precursor of most of the sphingolipids (sphingomyelin and glycosphingolipids) and are important for the early development of infants ^[67].

Cerebrosides

When a glucose/galactose moiety is attached to the ceramide, it is collectively called cerebrosides and is further classified as galactocerebrosides and glucocerebroside. They have a varied role and regulate signal transduction pathways, particularly in cell recognition/ adhesion/ proliferation and neuronal protection ^[88, 89]. These functional roles of polar lipids are fortified as nutraceuticals and functional foods for infants, children, elders, and athletes. Polar lipids are most commonly obtained from milk, rice bran oil, soybean, sunflower, and palm for commercial production ^[78].

Natural Preservatives

A preservative is a natural or synthetic material used to inhibit the growth of microorganisms and thereby prevent the decomposition or any undesirable chemical change in finished products ^[90]. They are commonly employed during the manufacturing of pharmaceuticals and cosmetics products due to their antibacterial, antifungal, and antioxidant properties [91-^{92]}. Preservatives are classified into two main classes: Artificial Preservatives and Natural Preservatives ^[93]. Natural preservatives are obtained from natural sources such as plants, animals, or certain microorganisms and their metabolites. Other than these natural preservatives, some techniques such as freeze-drying, heating, or desiccation also help in the preservation of the products. Natural preservation techniques can be classified as (1) inactivation of microorganisms, (2) hindering chemical deterioration (e.g., oxidation, enzymatic degradation) and microbial growth, (3) avoiding contamination.

Heating, Desiccation, Freeze Drying, Freezing

Heating and pasteurization are mainly mild heat treatments for milk and other dairy products. Sterilization is the process of rendering the product free of microorganisms. Autoclave at 121 °C or such a higher temperature produces the sterile product. However, food-like products would turn out to be of unacceptable quality at such a high temperature. Instead, it should be heat treated sufficiently to produce a shelf-stable and safe product.

Free water in food products supports the growth of microorganisms. Water activity is the amount of unbound

water available for microbial growth and chemical reactions. The reduction of water activity in food inhibits the growth of microbes, spore germination, and toxic byproducts formation by fungus and bacteria. Water activity can be significantly reduced by desiccation, freeze-drying technique, crystallization, and the addition of solutes that can react with free water of food. Low-temperature preservation, i.e., chilling or freezing of food products, nearly stops the clock for microbial growth as it stops the metabolic activity. Once the free water turns to ice, it does not support the growth of microorganisms ^[94-95].

Osmotic Dehydration

Osmotic dehydration involves the removal of free water from fresh foods by hypertonic solutions. The concentration of the hypertonic solution and solution temperature are important factors that determine the quality of the dehydrated product. Salt's ability to decrease water activity is thought to be due to the ability of sodium and chloride ions to associate with water molecules. Salt reduces water activity by drying out the food. Egyptian mummies were preserved with the concentrated brine solution, which osmotically drains the water from the body. Like salt, sugar also decreases water activity ^[96,97]. As water binds to sugar, it does not allow the microorganism to grow. Sweet pickles and jam are self-preserved as they are high in sugar content. Honey also acts as a viscous barrier to bacteria and other microorganisms. A high level of vegetable glycerin also acts similarly to sugar.

Antimicrobial Biopreservatives

The Biopreservation term indicates the use of natural microflora and its metabolites as a preservative for food to extend its shelf life. Bacteriocins produced from Lactic Acid Bacteria (LAB) act as preservatives. Nissin and diplococci are well-known bacteriocins. Nissin is approved by the FDA and is widely used in dairy product preservation ^[98-99]. Natamycin (pimaricin) is a tetraene polyene antibiotic - a natural antifungal medication obtained from soil bacteria *Streptomyces natalensis*. Highly potent natamycin binds to ergosterol, a building block in the cell wall of yeasts and molds. Once the natamycin binds to ergosterol, the transport pathway is blocked, and the cell dies.

Preservatives from Plant Source

Spices, herbs, and essential oils are added to food as a flavoring and aromatic agent. These essential oils have a varying degree of antimicrobial effect. They inhibit the growth of gram-positive, gram-negative bacteria, molds, fungi, and yeasts. The active compounds are generally the phenolic components of essential oil. Clove, oregano, rosemary, cinnamon, wasabi, thyme, sage, sweet basil, lemongrass, vanilla bean, cilantro, tea tree oil, onion, garlic, etc. have a major antimicrobial effect ^[100-102]. The preservatives obtained from plant sources are mentioned in Table 5 and Table 6.

Table 5: List of herbs used as preservative

		-	
Common Name	Scientific Name	Constituent	Use
		Essential oil: carvone, neo-	 Antifungal
Mountain Mint	Calamintha officinalis (Fam: Labiatae)	dihydrocarveol, 1,8 cineole	 Antimicrobial against
Wouldain Wint	Calaminina officinalis (Fall. Lablaide)	dihydrocarveol acetate, dihydrocarveol,	gram-positive bacteria
		cis-carvyl acetate, pulegone	 Antioxidant
Ceylon leadwort or	Plumbago zeylanica	Napthoquione: Plumbagin, Plumbagin	 Antifungal
Doctor bush	(Fam: <i>Plumbaginaceae</i>)	Napuloquione. Fiundagin, Piundagin	 Antibacterial

Tea tree	Melaleuca alternifolia (Fam: Myrtaceae)	Cineole, alpha-terpinene, gamma- terpinene, terpinolene, alpha-terpineol, terpinen-4-ol, limonene	AntimicrobialAntifungal
Cinnamon	Cinnamomum zeylanicum (Fam: Lauraceae)	Eugenol, camphor, α- and β-pinenes, β- caryophyllene, trans-cinnamyl acetate	 Antifungal Antiviral Bactericidal Larvicidal
Old man's beard, beard lichen	Usnea barbata (Fam:Parmeliaceae)	Usnic acid	 Antifungal
West Indian lemongrass	Cymbopogon citratus (Fam: Poaceae)	Citral, Citronellal, Dipentene, Myrecene	 Antifungal
Victorian eurabbie, Nilgiri	Eucalyptus globulus (Fam: Myrtaceae)	1,8-cineole, α-pinene, γ-terpinene and p- cymene	 Antifungal
Garlic	Allium sativum (Fam: Amaryllidaceae)	Volatile oil composed of diallyldisulfide, allyl methyl trisulfide, and diallyltrisulfide	 Antibacterial Anthelmintic Antifungal Antiviral
Barberry	Berberis vulgaris (Fam: Berberidaceae)	Berberine	 Antifungal
Cumin	Cuminum cyminum (Fam: Apiaceae)	Cuminaldehyde, cymene, terpenoids	AntifungalAntimicrobial

Table 6: List of essential oils used as Preservative

Name	Source	Chemical Constituents	Uses
Cardamom oil	Elettaria cardomomum (Fam: Zingiberaceae)	Methyl eugenol, terpenes	Antioxidant, relieve toothache and digestive disorder
Cinnamon oil	Cinnamomum zeylanicum (Fam: Lauraceae)	Eugenol, eugenol acetate and cinnamicacid, cinnamic aldehyde	Antioxidant, antiviral
Clove oil	Eugenia caryophylla (Fam: Myrtaceae)	Eugenol, Isoeugenol, Eugenol acetate	Antioxidant, antiviral, anthelmintic, toothache, hypoglycemic
Coriander	Coriandrum sativum (Fam: Umbelliferae)	Terpenes, linalool, and pinene	Antioxidant, antibacterial, anxiolytic, carminative
Eucalyptus oil	Eucalyptus globulus (Fam: Myrtaceae)	α -pinene, β -pinene, terpinen-4-ol, aromadendrene	Antioxidant, a cooling and deodorizing effect on the body,
Fennel oil	Foeniculum vulgare (Fam: Umbelliferae)	A-pinene, myrcene, limonene,1,8-cineole	Antioxidant, antiseptic, carminative, depurative, diuretic
Lemon oil	Citrus limonum (Fam: Rutaceae)	Ascorbic acid (vitamin c), a- terpinene, linalool, b- bisabolene,	Antioxidant, Antihypertensive
Thyme oil	Thymus vulgaris (Fam: Labiatae)	Thymol, a-thujone, a- pinene, linalool	Antioxidant, antiseptic, antifungal
Oregano oil	Origanum vulgare (Fam: Labiatae)	Phenolic acids and flavonoids	Antioxidant, antiviral, antibacterial

Preservatives from Animal Sources

Certain animal secretions or products produced outside or inside their bodies act as a source of preservation either in their crude form or processed to a suitable form. These secretions possess protective functions. The preservatives obtained from Animal sources are given in Table 7.

Name	Source	Uses
Chitosan	By Deacetylation of Chitin present in the exoskeleton of crustaceans (crabs, shrimps)	Natural Biopesticide
Defensin	Cysteine-rich cationic compounds found in both vertebrates and invertebrates and in plants	Antimicrobial against Fungi, Algae, enveloped and non-enveloped viruses
Lactoferrin/ Lacto transferrin	Found in Human Milk, Animal Milk, Saliva, Tears	Antibacterial, Antiviral, Antifungal, Anticancer
Lacto-peroxidase System	A Peroxidase enzyme secreted from mammary, salivary, and other mucosal glands	Antibacterial, Antiviral, Antitumour, Preservative
Lysozyme/ Muramidase	Found in Human Milk, Animal Milk, Saliva, Tears, neutrophils	Antibacterial (Gram-positive bacteria) Immunity Booster
Lard	Purified internal fat was obtained from the abdomen of hog Susscrofa Linn.	Preservative

Conclusion

Conventionally, the compounds that act as emulsifiers, natural preservatives, lipids, and natural surfactants are extracted directly from the natural sources that have their own limitations due to the low content of desired compounds and complicated separation procedures increase the cost of production. Thus, for commercial production, the use of renewable resources over fossil-based resources can provide tremendous advantages like protection to the environment, decreased production cost, and compounds with equal or improved yield. Also, by employing modern technologies like biotechnology, microbial fermentation techniques, and genetics, the non-utilizable biomass (crops and waste material) has been converted into much greener bio-based materials by microorganisms, which are equivalent to or superior to fossil-based materials.

References

- 1. John Wiley & Sons, editor. Kirk-Othmer Encyclopedia of Chemical Technology. Wiley; c2000.
- GRV GreenroomVoice. How biodegradable and biobased materials open up new opportunities in eco-design [Internet]. [Accessed October 25, 2021]. Available from: https://www.greenroomvoice.com/2019/04/howbiodegradable-and-bio-based-materials-open-up-newopportunities-in-eco-design/
- CEN-CENELEC. Standards for biobased products: new infographic developed by NEN [Internet]. [Accessed October 25, 2021]. Available from: https://www.cencenelec.eu/news-andevents/news/2021/briefnews/2021-06-29-standardsbiobased-products-new-infographic-nen/
 Crear Server @ for Sefer Chemicals Harred Accessment
- 4. GreenScreen® for Safer Chemicals Hazard Assessment Guidance. [Internet]. [Accessed date not provided]. Available from: [Insert URL if available]
- 5. Amulya K, Katakojwala R, Ramakrishna S, Venkata Mohan S. Low carbon biodegradable polymer matrices for sustainable future. Composites Part C: Open Access 2021; 4:100111.
- European Environment Agency. How much bioenergy can Europe produce without harming the environment? [Internet]. [Accessed October 25, 2021]. Available from: https://www.eea.europa.eu/publications/eea_report_2006_7
- Liang Y, Wen Z. Bio-based nutraceuticals from biorefining. Advances in Biorefineries, Elsevier; c2014, p. 596-623.
- 8. Johnson P, Trybala A, Starov V, Pinfield VJ. Effect of synthetic surfactants on the environment and the potential for substitution by biosurfactants. Advances in Colloid and Interface Science. 2021;288:102340.
- 9. Cui H, Cheetham AG, Pashuck ET, Stupp SI. Amino Acid Sequence in Constitutionally Isomeric Tetrapeptide Amphiphiles Dictates Architecture of One-Dimensional Nanostructures. Journal of the American Chemical Society. 2014;136:12461-8.
- Thavasi R, Subramanyam Nambaru VRM, Jayalakshmi S, Balasubramanian T, Banat IM. Biosurfactant Production by Pseudomonas aeruginosa from Renewable Resources. Indian Journal of Microbiology. 2011;51:30-6.
- 11. Bhadani A, Kafle A, Ogura T, Akamatsu M, Sakai K, Sakai H, *et al.* Current perspective of sustainable surfactants based on renewable building blocks. Current Opinion in Colloid & Interface Science. 2020;45:124-35.
- 12. Singh P, Patil Y, Rale V. Biosurfactant production: emerging trends and promising strategies. Journal of Applied Microbiology. 2019;126:2-13.
- Kapadia R, Parikh K, Jain M, Sawant K. Topical instillation of triamcinolone acetonide-loaded emulsomes for posterior ocular delivery: statistical optimization and *in vitro-in vivo* studies. Drug Delivery and Translational Research. 2021;11:984-99. DOI: 10.1007/s13346-020-00810-8.
- 14. Van Hamme JD, Singh A, Ward OP. Physiological aspects. Biotechnology Advances. 2006;24:604-20.
- 15. Nitschke M, Silva SS. Recent food applications of microbial surfactants. Critical Reviews in Food Science and Nutrition. 2018;58:631-8.

- Lawniczak L, Marecik R, Chrzanowski L. Contributions of biosurfactants to natural or induced bioremediation. Applied Microbiology and Biotechnology. 2013;97:2327-39.
- 17. Inès M, Dhouha G. Glycolipid biosurfactants: Potential related biomedical and biotechnological applications. Carbohydrate Research. 2015;416:59-69.
- De Graeve M, De Maeseneire SL, Roelants SLKW, Soetaert W. Starmerella bombicola, an industrially relevant, yet fundamentally underexplored yeast. FEMS Yeast Research. 2018;18:72.
- Rane AN, Baikar VV, Ravi Kumar DV, Deopurkar RL. Agro-industrial wastes for production of biosurfactant by Bacillus subtilis ANR 88 and its application in synthesis of silver and gold nanoparticles. Frontiers in Microbiology. 2017;8:1-12.
- 20. Rufino RD, De Luna JM, De Campos Takaki GM, Sarubbo LA. Characterization and properties of the biosurfactant produced by Candida lipolytica UCP 0988. Electronic Journal of Biotechnology. 2014;17:34-8.
- 21. Parmar M, Patel L, Hadia B, Rathod L, Parikh K. Lipidbased Nanocarriers of Tazarotene for the treatment of Psoriasis: Optimization and *In vitro* studies. World Journal of Pharmaceutical Research. 2019;8:1830-71.
- 22. Parikh KJ, Sawant KK. Comparative Study for Optimization of Pharmaceutical Self-Emulsifying Preconcentrate by Design of Experiment and Artificial Neural Network. American Association of Pharmaceutical Scientists Pharmaceutical Science and Technology. 2018;19:3311-21. DOI: 10.1208/s12249-018-1173-2.
- 23. Jahan R, Bodratti AM, Tsianou M, Alexandridis P. Biosurfactants, natural alternatives to synthetic surfactants: Physicochemical properties and applications. Advances in Colloid and Interface Science. 2020;275:102061.
- Parmar M, Patel L, Hadia B, Rathod L, Parikh K. Lipidbased Nanocarriers of Tazarotene for the Treatment of Psoriasis: Cell Cytotoxicity & *In vivo* Studies. International Journal of Pharmaceutical Sciences Review and Research. 2019;58:130-5.
- 25. Rojekar S, Abadi LF, Pai R, Prajapati MK, Kulkarni S, Vavia PR. Mannose-anchored nano-selenium loaded nanostructured lipid carriers of etravirine for delivery to HIV reservoirs. American Association of Pharmaceutical Scientists Pharmaceutical Science and Technology. 2022;23:230.
- 26. Ramos da Silva A, Manresa MÁ, Pinazo A, García MT, Pérez L. Rhamnolipids functionalized with basic amino acids: Synthesis, aggregation behavior, antibacterial activity and biodegradation studies. Colloids and Surfaces B: Biointerfaces. 2019;181:234-43.
- 27. Morya VK, Ahn C, Jeon S, Kim EK. Medicinal and Cosmetic Potentials of Sophorolipids. Mini-Reviews in Medicinal Chemistry. 2013;13:1761-8.
- 28. Haque F, Sajid M, Cameotra SS, Battacharyya MS. Antibiofilm activity of a sophorolipid-amphotericin B niosomal formulation against Candida albicans. Biofouling. 2017;33:768-79.
- 29. Wang J, Zhang J, Liu K, He J, Zhang Y, Chen S, *et al.* Synthesis of gold nanoflowers stabilized with amphiphilic daptomycin for enhanced photothermal antitumor and antibacterial effects. International Journal of Pharmaceutics 2020;580:119231.
- 30. Oliveira DML, Rezende PS, Barbosa TC, Andrade LN,

Bani C, Tavares DS, *et al.* Double membrane based on lidocaine-coated polymyxin-alginate nanoparticles for wound healing: *In vitro* characterization and *in vivo* tissue repair. International Journal of Pharmaceutics 2020;591:120001.

- 31. Aslam AA, Ishtaiq M, Badar R, Nazir MS, Tahir Z, Abdullah MA. Applications of biosurfactants in the production of industrially relevant bioproducts. Green Sustainable Process for Chemical and Environmental Engineering and Science, Elsevier; c2021. p. 173-201.
- 32. Kumar S, Sharma B, Bhadwal P, Sharma P, Agnihotri N. Lipids as Nutraceuticals: A Shift in Paradigm. Therapeutic Foods, Elsevier; c2018. p. 51-98.
- 33. Forde CJ, Meaney M, Carrigan JB, Mills C, Boland S, Hernon A. Biobased Fats (Lipids) and Oils from Biomass as a Source of Bioenergy. Bioenergy Research: Advances and Applications, Elsevier; c2014. p. 185-201.
- 34. Gibson M, Newsham P. Food Science and the Culinary Arts. Elsevier; c2018.
- 35. Schwingshackl L, Hoffmann G. Monounsaturated Fatty Acids and Risk of Cardiovascular Disease: Synopsis of the Evidence Available from Systematic Reviews and Meta-Analyses. Nutrients. 2012;4:1989-2007.
- 36. Ander BP, Dupasquier CM, Prociuk MA, Pierce GN. Polyunsaturated fatty acids and their effects on cardiovascular disease. Experimental and Clinical Cardiology. 2003;8:164-72.
- 37. Kaur N, Chugh V, Gupta AK. Essential fatty acids as functional components of foods- a review. Journal of Food Science and Technology. 2014;51:2289-303.
- 38. Itsiopoulos C, Marx W, Mayr HL, Tatucu-Babet OA, Dash SR, George ES, *et al.* The role of omega-3 polyunsaturated fatty acid supplementation in the management of type 2 diabetes mellitus: A narrative review. Journal of Nutrition and Intermediary Metabolism. 2018;14:42-51.
- Siemionow M, Kulahci Y, Agaoglu G. Diabetic Neuropathy: Pathogenesis and Treatment. Oxidative Stress and Neurodegenerative Disorders, Elsevier; c2007. p. 543-79.
- Jin M, Zhai R, Xu Z, Wen Z. Production of High-Value Polyunsaturated Fatty Acids Using Microbial Cultures. Methods in Molecular Biology, vol. 1995, Humana Press Inc.; c2019. p. 229-48.
- 41. Zehr KR, Walker MK. Omega-3 polyunsaturated fatty acids improve endothelial function in humans at risk for atherosclerosis: A review. Prostaglandins Other Lipid Mediat. 2018;134:131-40.
- 42. Ochi E, Tsuchiya Y. Eicosapentaenoic Acid (EPA) and Docosahexaneoic Acid (DHA) in Muscle Damage and Function. Nutrients. 2018;10:552.
- 43. McKenney JM, Sica D. Role of Prescription Omega-3 Fatty Acids in the Treatment of Hypertriglyceridemia. Pharmacotherapy. 2007;27:715-28.
- 44. Sublette ME, Ellis SP, Geant AL, Mann JJ. Meta-Analysis of the Effects of Eicosapentaenoic Acid (EPA) in Clinical Trials in Depression. Journal of Clinical Psychiatry. 2011;72:1577-84.
- 45. Chavarro JE, Stampfer MJ, Li H, Campos H, Kurth T, Ma J. A Prospective Study of Polyunsaturated Fatty Acid Levels in Blood and Prostate Cancer Risk. Cancer Epidemiology Biomarkers & Prevention. 2007;16:1364-70.
- 46. Ramos-Campo DJ, Ávila-Gandía V, López-Román FJ, Miñarro J, Contreras C, Soto-Méndez F, *et al.*

Supplementation of Re-Esterified Docosahexaenoic and Eicosapentaenoic Acids Reduce Inflammatory and Muscle Damage Markers after Exercise in Endurance Athletes: A Randomized, Controlled Crossover Trial. Nutrients. 2020;12:719.

- 47. Gandhi M, Misra A, Mashru R. Lipoplex delivery system for P11 gene: a risk-based quality by design approach; c2018.
- Gema A, Kavadia D, Dimou V, Tsag H. Production of γlinolenic acid by Cunninghamella echinulata cultivated on glucose and orange peel. Applied Microbiology and Biotechnology. 2002;58:303-7.
- 49. Eroshin VK, Dedyukhina EG, Chistyakova TI, Zhelifonova VP, Kurtzman CP, Bothast RJ. Arachidonicacid production by species of Mortierella. World Journal of Microbiology and Biotechnology. 1996;12:91-6.
- 50. Okuda T, Ando A, Negoro H, Muratsubaki T, Kikukawa H, Sakamoto T, *et al.* Eicosapentaenoic acid (EPA) production by an oleaginous fungus Mortierella alpina expressing heterologous the $\Delta 17$ -desaturase gene under ordinary temperature. European Journal of Lipid Science and Technology. 2015;117:1919-27.
- Hoshida H, Ohira T, Minematsu A, Akada R, Nishizawa Y. Accumulation of eicosapentaenoic acid in *Nannochloropsis* sp. in response to elevated CO₂ concentrations. Journal of Applied Phycology. 2005;17:29-34.
- 52. Gandhi SR, Weete JD. Production of the polyunsaturated fatty acids arachidonic acid and eicosapentaenoic acid by the fungus Pythium ultimum. Journal of General Microbiology. 1991;137:1825-30.
- 53. Yazawa K. Production of eicosapentaenoic acid from marine bacteria. Lipids. 1996;31:S297-300.
- 54. Yu R, Yamada A, Watanabe K, Yazawa K, Takeyama H, Matsunaga T, *et al.* Production of eicosapentaenoic acid by a recombinant marine cyanobacterium, *Synechococcus* sp. Lipids. 2000;35:1061-4.
- 55. Zhu. High eicosapentaenoic acid producing strains of Yarrowia lipolytica. US7932077B2; c2005.
- 56. Ren LJ, Ji XJ, Huang H, Qu L, Feng Y, Tong QQ, et al. Development of a stepwise aeration control strategy for efficient docosahexaenoic acid production by *Schizochytrium* sp. Applied Microbiology and Biotechnology. 2010;87:1649-56.
- 57. Ratledge C, Kanagachandran K, Anderson AJ, Grantham DJ, Stephenson JC. Production of docosahexaenoic acid by Crypthecodinium cohnii grown in a pH-auxostat culture with acetic acid as principal carbon source. Lipids. 2001;36:1241-6.
- 58. Turpeinen A, Merimaa P. Functional fats and spreads. Functional Foods, Elsevier; c2011. p. 383-400.
- 59. Bot A. Phytosterols. Encyclopedia of Food Chemistry, Elsevier; c2019. p. 225-8.
- 60. Tamura T, Akihisa T, Kokke W. Naturally Occurring Sterols and Related Compounds from Plants. Physiology and Biochemistry of Sterols, AOCS Publishing; c1992. p. 172-228.
- 61. Jesch ED, Carr TP. Food Ingredients That Inhibit Cholesterol Absorption. Preventive Nutrition and Food Science. 2017;22:67-80.
- Parikh KJ, Sawant KK. Solubilization of vardenafil HCl in lipid-based formulations enhances its oral bioavailability *in vivo*: A comparative study using Tween - 20 and Cremophor - EL. Journal of Molecular Liquids 2019;277:189-99.

DOI: 10.1016/J.MOLLIQ.2018.12.079.

- 63. Katan MB, Grundy SM, Jones P, Law M, Miettinen T, Paoletti R. Efficacy and Safety of Plant Stanols and Sterols in the Management of Blood Cholesterol Levels. Mayo Clinic Proceedings. 2003;78:965-78.
- 64. Plat J, Brufau G, Dallinga-Thie GM, Dasselaar M, Mensink RP. A Plant Stanol Yogurt Drink Alone or Combined with a Low-Dose Statin Lowers Serum Triacylglycerol and Non-HDL Cholesterol in Metabolic Syndrome Patients. Journal of Nutrition. 2009;139:1143-9.
- 65. Salehi B, Quispe C, Sharifi-Rad J, Cruz-Martins N, Nigam M, Mishra AP, *et al.* Phytosterols: From Preclinical Evidence to Potential Clinical Applications. Frontiers in Pharmacology. 2021;11:1819.
- 66. Spector AA, Yorek MA. Membrane lipid composition and cellular function. Journal of Lipid Research 1985;26:1015-35.
- Zheng L, Fleith M, Giuffrida F, O'Neill BV, Schneider N. Dietary Polar Lipids and Cognitive Development: A Narrative Review. Advances in Nutrition. 2019;10:1163-76.
- 68. Farooqui AA, Horrocks LA, Farooqui T. Glycerophospholipids in brain: their metabolism, incorporation into membranes, functions, and involvement in neurological disorders. Chemistry and Physics of Lipids. 2000;106:1-29.
- 69. William S. An introduction to biological membranes: from bilayers to rafts, Elsevier/Academic Press; c2013. p. 367.
- Vemulapalli S, Hashemi M, Kolomeisky AB, Lyubchenko YL. Assembly of Synaptic Protein-DNA Complexes: Critical Role of Non-Specific Interactions. International Journal of Molecular Sciences. 2023;24:9800.
- 71. Moolenaar WH, Kruijer W, Tilly BC, Verlaan I, Bierman AJ, De Laat SW. Growth factor-like action of phosphatidic acid. Nature. 1986;323:171-3.
- 72. Calzada E, Onguka O, Claypool SM. Phosphatidylethanolamine Metabolism in Health and Disease. International Review of Cell and Molecular Biology. 2016;321:29-88.
- Vance J, Steenbergen R. Metabolism and functions of phosphatidylserine. Progress in Lipid Research. 2005;44:207-34.
- 74. Kim HY, Huang BX, Spector AA. Phosphatidylserine in the brain: metabolism and function. Progress in Lipid Research. 2014;56:1-18.
- 75. Toker A. Phospholipids | Phosphatidylinositol Bisphosphate and Trisphosphate. Encyclopedia of Biological Chemistry III, Elsevier; c2013. p. 552-6.
- 76. Okano G, Akino T. Variations in the molecular species of lung phosphatidylglycerol. Lipids. 1979;14:541-6.
- 77. Chaung HC, Chang CD, Chen PH, Chang CJ, Liu SH, Chen CC. Docosahexaenoic acid and phosphatidylserine improves the antioxidant activities *in vitro* and *in vivo* and cognitive functions of the developing brain. Food Chemistry. 2013;138:342-7.
- Le TT, Phan TTQ, Van Camp J, Dewettinck K. Milk and Dairy Polar Lipids: Occurrence, Purification, and Nutritional and Technological Properties. Polar Lipids, Elsevier; c2015. p. 91-143.
- 79. Hellhammer J, Waladkhani A, Hero T, Buss C. Effects of milk phospholipid on memory and psychological stress response. British Food Journal. 2010;112:1124-37.

- 80. Küllenberg D, Taylor LA, Schneider M, Massing U. Health effects of dietary phospholipids. Lipids in Health and Disease. 2012;11:3.
- 81. Buccoliero R, Bodennec J, Futerman AH. The role of sphingolipids in neuronal development: lessons from models of sphingolipid storage diseases. Neurochemical Research. 2002;27:565-74.
- Gurnida DA, Rowan AM, Idjradinata P, Muchtadi D, Sekarwana N. Association of complex lipids containing gangliosides with cognitive development of 6-month-old infants. Early Human Development. 2012;88:595-601.
- Don AS, Hsiao JHT, Bleasel JM, Couttas TA, Halliday GM, Kim WS. Altered lipid levels provide evidence for myelin dysfunction in multiple system atrophy. Acta Neuropathologica Communications. 2014;2:150.
- 84. Litwack G. Lipids. Human Biochemistry, Elsevier; c2018. p. 199-255.
- 85. Sang S, Zhu Y. Bioactive Phytochemicals in Wheat Bran for Colon Cancer Prevention. Wheat and Rice in Disease Prevention and Health, Elsevier; c2014. p. 121-9.
- 86. Vakar, Mazumder R, Padhi S, Tiwari KS, Parikh K. Development of Colon Targeting Tablet of a JAK Inhibitor to Combat Chronic Ulcerative Colitis: A Novel Approach for Local Drug Delivery. Indian Journal of Pharmaceutical Education and Research. 2021;55:414-27.
- Jesch ED, Carr TP. Food Ingredients That Inhibit Cholesterol Absorption. Preventive Nutrition and Food Science. 2017;22:67-80.
- Hannun YA, Obeid LM. Principles of bioactive lipid signalling: lessons from sphingolipids. Nature Reviews Molecular Cell Biology. 2008;9:139-50.
- 89. Young MM, Kester M, Wang HG. Sphingolipids: regulators of crosstalk between apoptosis and autophagy. Journal of Lipid Research. 2013;54:5-19.
- 90. Tiwari BK, Valdramidis VP, Bourke P, Cullen P. Application of plant-based antimicrobials in food preservation. Natural Antimicrobials in Food Safety and Quality, Wallingford: CABI; c2011. p. 204-23.
- Mucklow JC. Martindale: The Complete Drug Reference. British Journal of Clinical Pharmacology. 2000;49:613-613.
- 92. Boyce MC, Spickett EE. Separation of Food Grade Antioxidants (Synthetic and Natural) Using Mixed Micellar Electrokinetic Capillary Chromatography. Journal of Agricultural and Food Chemistry. 1999;47:1970-5.
- 93. Singh A, Sharma P, Garg G. Natural products as preservatives. International Journal of Pharma and Bio Sciences; c2010.
- 94. Gandhi M, Bhatt P, Chauhan G, Gupta S, Misra A, Mashru R. IGF-II-Conjugated Nanocarrier for Brain-Targeted Delivery of p11 Gene for Depression. American Association of Pharmaceutical Scientists Pharmaceutical Science and Technology. 2019;20:50.
- 95. Gandhi M, Pandya T, Gandhi R, Patel S, Mashru R, Misra A, *et al.* Inhalable liposomal dry powder of gemcitabine-HCI: Formulation, *in vitro* characterization and *in vivo* studies. International Journal of Pharmaceutics. 2015;496:886-95.
- 96. Parmar C, Parikh K, Mundada P, Bhavsar D, Sawant K. Formulation and optimization of enteric coated bilayer tablets of mesalamine by RSM: *In vitro - In vivo* investigations and roentgenographic study. Journal of Drug Delivery Science and Technology. 2018;44:388-98.

DOI: 10.1016/J.JDDST.2018.01.008.

- 97. Parikh K, Mundada P, Sawant K. Design and Optimization of Controlled Release Felbamate Tablets by D-optimal Mixture Design: *In vitro-in vivo* Evaluation. Indian Journal of Pharmaceutical Sciences. 2019;81:71-81.
- Patil S, Prajapati B, Pandey A, Parikh K, Sawant K. Parenteral Controlled Drug Delivery Systems; c2023. p. 382-419.
- 99. Parikh K, Patel M, Mandal JK. Liquid parenteral compositions of levothyroxine; c2021.
- 100.Parikh K, Kapadia R, Pai R, Prajapati M, Shevalkar G. Emerging Formulation Technologies Against Malaria Resurgence. Drug Development for Malaria; c2022. p. 45-82. DOI: 10.1002/9783527830589.ch3.
- 101.Kamani P, Parikh K, Kapadia R, Sawant K. Phospholipid based ultra-deformable nanovesicular gel for transcutaneous application: QbD based optimization, characterization and pharmacodynamic profiling. Journal of Drug Delivery Science and Technology. 2019;51:152-63. DOI: 10.1016/J.JDDST.2019.02.035.
- 102. Parikh KJ, Christian JR, Rajpoot K, Tekade RK. Chapter
 22 Environmental and safety aspects of bionanotechnology. In: Tekade RK, editor. Pharmacokinetics and Toxicokinetic Considerations, vol. 2, Academic Press; c2022. p. 605-50. DOI: 10.1016/B978-0-323-98367-9.00022-6.