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Synergistic Elegance: Harnessing Liposomes as Advanced Cosmetic Drug Delivery Systems with Phospholipids and Phenolic Components

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Abstract

Liposomes, widely embraced for their safety in cosmetic applications, have become integral to the beauty industry. Derived from biologically sourced phospholipids, these compounds exhibit a remarkable affinity for the skin's surface. Not only are liposomes highly permeable, with significant storage capacity in the stratum corneum, but they also act as dynamic agents on the skin. On-going research in liposomes primarily focuses on their potential in cosmetic drug delivery. Formulations of liposomes, sourced from diverse phospholipid origins such as egg and soya, undergo differentiation based on their impact on skin parameters, including water content, elasticity, and barrier function. The diverse array of phospholipids within liposomes contributes to a spectrum of effects on human skin. Phenolic compounds derived from plant metabolites present antioxidant and anti-inflammatory activities. However, the stability and bioactivity of these compounds are contingent upon careful extraction processes, given their sensitivity to light and heat sources. Challenges such as rapid metabolization, low solubility, and limited bioavailability characterize phenolic compounds. This article not only imparts valuable insights into the role of liposomes, particularly those containing phospholipids and phenolic compounds, in cosmetics but also sheds light on innovative methods in liposome formulation. Additionally, it delves into a discussion about liposomes already present in the cosmetic market, offering a comprehensive overview of their potential and current applications in the beauty industry.

Keywords: Liposomes; Phospholipids; Phenolic Compounds; Cosmetics

Abbreviations

PCL: Polycaprolactone; EGCG: Epigallocatechin-3-Gallate; DLS: Dynamic Light Scattering; CHWPE: Cocoa Hull Waste Phenolic Extract; NMR: Nuclear Magnetic Resonance; CUPRAC: Cupric Reducing Antioxidant Capacity; DSC: Differential Scanning Calorimetry; FTIR: Fourier-Transform Infrared Spectroscopy; DPPH: 2,2-Diphenyl-1-Picrylhydrazyl.

Introduction

In the 1960s, Dr. Bangham AD [1] and his collaborators at the Babraham Institute, University of Cambridge, made a ground breaking discovery by identifying liposomes [1]. These spherical vesicles are characterized by one or more concentric bilayer phospholipids, encapsulating an aqueous core. The realm of cosmetics has witnessed numerous studies on the application of topical agents. Notably, in Japan, investigations into cutaneous absorption paved the way for regulatory agencies to oversee the safety and stability of liposome products. The application of liposomes in skin treatments is rooted in the bilayer structure of lipid vesicles, akin to natural membranes [2]. This structure, depending on lipid composition, empowers lipid vesicles to modulate cell membrane fluidity and facilitate fusion with cells, thereby delivering active drugs to the target site. Ethanol, a component in lipid vesicle systems known as Ethosomes, has been observed to influence skin (Stratum Corneum) penetration and drug permeation within the system. This research significantly adds to our knowledge regarding the improvement of liposome penetration and the impact of drugs on the skin. The insights gleaned from these studies provide valuable information for refining approaches to enhance the efficacy of liposomes in delivering therapeutic agents through the skin. Understanding the intricacies of liposome-skin interactions not only improves the potential for targeted drug delivery but also creates opportunities for developing innovative formulations in dermatology and cosmetics. Liposomal formulations are extensively utilized in cosmetics and dermatology applications to balance the skin's moisture levels [3].

In the cosmetic industry, the incorporation of phenolic compounds into liposomal formulations marks a significant improvement. The process involves the solvent-free extraction of phenolic compounds, characterized by their solvent-free nature and absence of residues. Phenolic compounds, known for their low solubility and rapid metabolization, exhibit enhanced bioavailability. Their anti-inflammatory mechanisms play a crucial role in terminating inflammatory responses, facilitating a return to homeostasis. In the realm of liposomal drug delivery for cosmetics, various factors come into play, including solubility, shape, size, melting point, and purity. Understanding and optimizing these factors contribute to the efficacy of liposomal formulations in delivering cosmetic actives with precision and efficiency [4].

Liposome design plays a pivotal role in creating effective formulations, encompassing the choice of composition, functionalization, and targeting approaches. The selection of phospholipids, including their head group, chain length, and component ratios, is crucial for ensuring liposome safety, stability, and efficiency. Various factors such as the quantity and rigidity of lipid bilayers, size, surface charge, lipid organization, and surface modification can impact the distribution of drugs by liposomes [5].

The properties of phospholipid compounds, commonly sourced from natural materials like soybeans and egg yolk, are vital for cosmetic applications. While soy phospholipids offer cost efficiency, egg yolk's high phosphatidylcholine content contributes emulsification effects. Natural phospholipids, containing unsaturated fatty acids, pose challenges to storage stability. To maintain stability in cosmetics, strategies must address oxidation, physical changes like condensation and sedimentation, as well as chemical changes like color and smell alterations and lipid decomposition. Oxidation stability can be enhanced by factors such as hydrogenation and maintaining low peroxide values [6].

Glycerophospholipids, characterized by a glycerol molecule linked to a phosphate group and two saturated fatty acids, are the major components of liposomes. Different types of natural phospholipids, such as phosphatidic acid, phosphatidylcholine, phosphatidylethanolamine, phosphatidylinositol, phosphatidylglycerol, and phosphatidylserine, define this chemical group. Liposomes, categorized by lamellarity and vesicle size, can be unilamellar, multilamellar, or multivesicular vesicles. The number of lamellae and vesicle size influence the amount of compounds encapsulated [7].

Phenolic compounds, inherently stable and bioactive in plants, face challenges in extraction due to factors like pH and oxygen. Their bioavailability is hampered by low solubility in biological fluids and rapid in vivo metabolization. Various formulations, including liposomes, nanoparticles, and emulsions, aim to enhance solubility and bioavailability. The application of phenolic compounds in cosmetics addresses skin pigmentation, aging, sun exposure effects, and even exhibits anticancer properties [8].

Innovative liposome preparation methods are under exploration for industrial scalability and applicability to diverse phospholipids and drugs. Methods like cross-flow injection, membrane contactor technology, and supercritical fluid techniques, particularly using carbon dioxide, offer advantages such as cost-effectiveness, environmental friendliness, and controlled particle size. The future potential of these novel methods in therapeutic and pharmacological applications is promising, paving the way for advancements in liposome technology [9].

Method	Main Characteristic
Cross-flow injection	(A) Simple, Measurable, Sterile and continuous Process
	(D) organic solvent residue leads to stability problem
Membrane Contract	(A) Simple, Measurable, Sterile and continuous Process
	(D) High cost, not suitable for hydrophilic drug
Cross-flow filtration	(A) Simple, Measurable, Sterile and continuous Process, Rapid
	(D) understudy method
RESS	(A) Simple, fast, Solvent Free process
	(D) Low yield
GAS	(A) Small & stable
	(D) Batch process
SAS	(A) Single step process
	(D) Difficult to optimize Condition
ASES	(A) One step process with Measurable
	(D) Heterogeneous and understudy process
SCRPE	(A) Simple and Reproducible Process,
	(D) High cost

Table 1: The Main Characteristics, (A) Advantages and (D) Disadvantages.

Evaluation of Liposomal Phenolics Bioactivity In-vitro: Numerous in-vitro studies underscore the beneficial effects of phenolic-loaded liposomes on the body, showcasing approved activities such as antitumor (against various tumour types), antioxidant, anti-inflammatory, antimicrobial, and neuroprotective properties [10]. The efficacy of these liposomes is influenced by factors such as their size, phase transition temperature, pH, zeta potentials, bio accessibility, low toxicity, release rate, and antioxidant capacity. These parameters play a crucial role in determining the release rate of compounds and their antioxidant properties, indicating the stability of liposomes against oxidation even at elevated temperatures, making them excellent carriers for bioactive compounds [11].

A study conducted by Pires et al. (2019C) explored the antioxidant properties of polycaprolactone (PCL) prepared via the electrospinning method and incorporated liposomes loaded with epigallocatechin-3-gallate (EGCG) [12]. This formulation aimed to enhance wound healing and promote skin tissue regeneration. Results indicated that EGCG effectively scavenged toxic species generated by exposure to ultraviolet radiation, slowing down oxidation events and minimizing damage. In another study, chitosan encapsulation-coated liposomes loaded with cacao demonstrated a sixfold increase in bio accessibility during in-vitro digestion, emphasizing the potential of this formulation [13].

Maintaining high cholesterol to phospholipid ratio (e.g., 70:30) contributes to the stability of liposomes, resulting in a controllable and reproducible formulation. The use of phospholipids with a high transition temperature (around 42-45°C) further enhances stability. Loading phenolic molecules into lipid-based nanocarriers has been shown to reduce toxicity, with lipids being considered favourable materials for encapsulating phenolic components due to their hydrophobic nature and suitability for industrial production [14,15].

Studies involving encapsulated phenolic molecules from *Spirulina sp*. LEB-18 in DMPC liposomes demonstrated a slower release rate compared to free phenolic extract [16]. Baicalein encapsulated in liposomes exhibited no cytotoxic effects on PC12 and SHSY5 cells. Similarly, a liposomal curcumin formulation demonstrated low toxicity to synovial fibroblasts and macrophages compared to free curcumin, showcasing its potential for the treatment of various diseases. This formulation not only reduced inflammatory cytokine/chemokine expression in synovial fibroblasts but also preserved cell viability [17].

In conclusion, these studies affirm that phenolic-loaded liposomes offer promising prospects in terms of stability, bioavailability, and reduced toxicity, making them a valuable avenue for the development of innovative therapeutic formulations.

Type of Study	Compound	Technique	Parameter & Instrumentation	Results
***In-Vitro* Study**	Polyphenolic grape seed extract	High-pressure Homogenization	Size, Dynamic Light Scattering (DLS)	Increased size ranges from 40-100 nm,
	Annona muricata L. extraction from aqueous solution	Hydration of bilipid layer	pH, DLS	3.8
	EGCG	Homogenization Technique	Zeta potential, DLS	Mean potential of empty liposome 45 mV
	Cocoa hull waste phenolic extract (CHWPE)	Spray-drying	Bio accessibility, CUPRAC assay	Increased at least 6-fold
	Spirulina sp LEB-18 Phenolic extract	Hydration of lipid bilayer	Release rate, FTIR, NMR, DSC	Slow-release rate
	Curcumin	Film technique	Antioxidant technique, DPPH assay	Inhibition of lipopolysaccharide

Table 2: The *In-Vitro* Studies Summarization.

Evaluation of Liposomal Phenolics Bioactivity In-vivo: Several properties, including low toxicity, increased stability, and anti-inflammatory effects, were investigated in liposomes loaded with syringic acid. These liposomes were synthesized with an average diameter size of 40.01±0.48 nm using a light-scattering instrument methodology [18]. The small particle size was found to have a direct impact on in-vivo time and distribution. Another study evaluated the size of liposomes containing liquorice extraction from liquorice roots. These vesicles were all below 100 nm, exhibiting a highly negative zeta potential range of −32 ± 2 mV, ensuring long-term stability and the capacity to incorporate a high amount of the extract. The liposomes maintained a uniform, loose, and full appearance [19]. Biochemical assays demonstrated a hepatoprotective effect against CCl_4-induced liver injury. CCl_4, a well-known hepatotoxin generating free radicals, was studied in experimental liver disease models. Mice injected with liposomes showed no toxicity after several doses, and rats injected with different doses (10, 25, or 100 mg/kg) exhibited no adverse effects [20]. The liposomes loaded with licorice extraction also demonstrated an anti-inflammatory effect, reducing TPA-induced neutrophil infiltration and promoting epidermal regeneration in mice. TPA, applied topically on mouse skin, induces inflammation, ulceration, oxidative stress, inflammatory cell infiltration, horny layer loss, and edema, with a significant reduction observed in edema [21].

In-vivo studies on mice highlighted the potential of nano systems to enhance the efficacy of extractions, particularly in improving re-epithelization. Biochemical and histological studies of syringic acid-loaded liposomes indicated improvements in the activities of antioxidant enzymatic and non-enzymatic systems, leading to a reduction in lipid peroxidation in the liver [22]. Additionally, rosemary extraction encapsulated through liposomes using the extrusion technique exhibited antioxidant properties. This formulation decreased xanthine oxidase-dependent lipid peroxidation, preventing the formation of anion radicals and inhibiting oxidation by up to 60%. The fluorescent intensity assay using the probe DPH-PA was employed to study the scavenging property of phenolic compounds against free radicals. These in-vivo studies collectively demonstrate the potential benefits of liposomal formulations in various biological activities (Table 3) [23].

Type of Study	Compound	Technique	Parameter & Instrumentation	Results
In-vivo study	Syringic acid	Thin-film dispersion method	Size, Light- scattering instrument	40.01±0.48 nm
	Liquorice extract from *Glycyrrhiza glabra* L. roots	Hydration of the bilipid layer	Size, Light- scattering instrument charge DLS	Mean diameter increased from 71 ± 2 to 100 ± 6 nm
	DOPE derivatives	Extrusion		Negative charge is involved in prolonging the circulation time
	Chlorogenic acid	Film drying method	Toxicity Biochemical assays	Hepatoprotective effects against CCl4-induced liver injury
	Syringic acid	Thin-film dispersion method	Biochemical and histological studies	Improvement of the activities of antioxidant enzymatic and no enzymatic system
	Rosmary extract	Extrusion	Antioxidant activity	Suppresses the xanthine oxidase-dependent lipid peroxidation

Table 3: The *In-Vitro* Studies Summarization.

Industrial Application: Encapsulation techniques play a crucial role in various industries, including food and beverage, cosmetics, pharmaceuticals, agriculture, chemicals, biotechnology, and biomedicine. In the food and beverage industry, liposomes are employed to reduce nutritional and sensory losses of anthocyanins, extending their stability during production, storage, and consumption [24]. This protective barrier shields bioactive compounds from environmental conditions and degradation within the digestive system. In the pharmaceutical sector, quercetin-loaded liposomes act as potent oxygen radical scavengers, particularly beneficial in diseases involving oxidative stress. These liposomes are valued for their non-toxic nature, biodegradability, and lack of immunogenic properties, facilitating the delivery of encapsulated drugs to target organs. In the cosmetic industry, liposomes loaded with anthocyanins, chosen for their high lipid profile, ensure protection of compounds and enhance skin absorption [25].

Since 2008, liposomes have been the predominant nanoparticles in the market, making a significant impact on various industries. The primary objective of encapsulation is to serve as a protective barrier against environmental factors, control release kinetics, and prolong the product's shelf life. In dermatological applications, liposomes offer numerous advantages, including reduced side effects, enhanced drug accumulation in the skin, non-toxic and biodegradable characteristics, scalability for manufacturing, ability to encapsulate both water and lipid-soluble components, water-resistant properties, moisturizing and restoring skin lipids, and localized drug depots within the skin [26].

In an in-vivo study, quercetin and resveratrol-loaded liposomes demonstrated tissue damage amelioration in a mouse model with skin lesions. This led to a reduction in edema and leukocyte infiltration, indicating potential therapeutic applications for diseases associated with inflammation and oxidative stress, including precancerous skin lesions. Various cosmetic products utilize encapsulation techniques, such as shower and bath gels, moisturizers, hair products, sunscreens, tanning creams, makeup, perfumes, soaps, exfoliants, and toothpaste [27]. Commercial products formulated with liposomes loaded with phenolic compounds showcase the versatility and applicability of encapsulation in the cosmetic industry are shown on Table 4. Sesderma® offers two distinct serums featuring phenolic compounds such as ferulic acid, resveratrol, and quercetin encapsulated within liposomes. These serums aim to prevent and treat facial photoaging, dehydration, wrinkles, and skin spots [28].

Another notable product is the mask from Decorté®, incorporating liposomes and anthocyanins from Murasaki-Kuromai (purple rice). This formulation serves a hydrating function to revitalize fatigued skin, counteracting dullness and rough texture caused by skin oxidation from environmental damage. Additionally, Mythos® presents a skin rejuvenate cream containing anthocyanins sourced from pomegranate extract. This product aims to promote skin regeneration, smooth wrinkles, and enhance skin elasticity, offering protection against oxidative stress and adverse environmental factors [29].

The Age Defense Eye Cream from Apivita® is another noteworthy product, utilizing anthocyanins from secretion encapsulated in liposomes. This eye cream contributes to skin regeneration, wrinkle smoothing, and increased skin elasticity while safeguarding against oxidative stress and environmental factors. Each of the mentioned products features liposomes with different sizes, as outlined in Table 4. Despite the variations, all liposomes fall within the range of 50 to 500 nm, showcasing the diversity in liposomal formulations across these skincare products [30,31].

Product/ Brand	Compound	Natural source	Liposome Size
Ferulac Liposomal Serum by Sesderma ®	Ferulic acid	Apple polyphenol extract	80-120 nm
Resveraderm Antiox Serum by Sesderma ®	Resveratrol, quercetin and EGCG	Red grape extract	80-120 nm
Moisture Liposome Mask by Decorté ®	Anthocyanins	Murasaki-Kuromai (purple rice) extract	1l00 nm
Skin rejuvenate cream by Mythos ®	Anthocyanins	*Punica granatum* (pomegranate) extract	50-500 nm
Holistic Age Defense Eye Cream Apivita ®	Anthocyanins	Greek royal jelly extract	70-100 nm

Table 4: Commercial Products Formulated With Loaded Liposomes with Phenol Compounds.

Conclusion

Liposomes have emerged as a versatile drug delivery system for a wide array of drugs, playing a crucial role in the development of innovative liposomal formulations for both diagnosis and treatment across various diseases. The application of liposomes in drugs extends to creative formulations that enhance the therapeutic effects of pharmaceutical compounds. The molecules chosen for encapsulation in liposomes serve as essential components, contributing to the effectiveness of drug delivery systems. In the cosmetic industry, liposomes play a pivotal role in facilitating the delivery of cosmetic components. Incorporating phenolic components in liposomal formulations improves bioavailability, stability, and encapsulation, thereby enhancing the overall characterization of cosmetic products.

Cosmetic products utilizing liposomes gain a distinct advantage in penetrating the stratum corneum, the outermost layer of the skin. Liposomes, particularly those prepared from phospholipids, contribute to increased skin water content. This property proves advantageous for dermatologists, offering enhanced moisturization and skin hydration. Liposome formulations are integral to the moisturization of the skin, and the use of egg phospholipids in topical preparations for cosmetic drug delivery systems is particularly noteworthy. This strategic choice contributes to an increase in skin water content, providing a significant advantage in cosmetic formulations aimed at promoting skin health and aesthetics. These advancements in liposomal technology underscore the importance of continuous innovation in the cosmetic and pharmaceutical industries.

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Conflicts of Interest: Nil

References

1. Bangham AD, Horne RW (1964) Negative staining of phospholipids and their structural modification by surface-active agents as observed in the electron microscope. J Mol Biol 8: 660-668.

2. Sebaaly C, Greige-Gerges H, Stainmesse S, Fessi H and Charcosset C (2016) Effect of composition, hydrogenation of phospholipids and lyophilization on the characteristics of eugenol-loaded liposomes prepared by ethanol injection method. Food Biosci 15: 1-10.

3. Gregoriadis G (1994) Liposomes and anti-aging creams: the facts beneath the face. Biochemist.

4. Touitou E, Dayan N, Bergelson L, Godin B, Eliaz M (2000) Ethosomes-novel vesicular carriers for enhanced delivery: characterization and skin penetration properties. J Control Rel 65(3): 403-418.

5. Sapkale G, Patil S, Surwase U, Bhatbhage P (2019) Supercritical Fluid Extraction: A Review. J Biol Chem

5(1): 114-122.

6. Bonechi C, Martini S, Ciani L, Lamponi S, Rebmann H, Rossi C, et al. (2012) Using Liposomes as Carriers for Polyphenolic Compounds: The Case of Trans Resveratrol. PLoS ONE 7(8): 41438.

7. Antunes-Ricardo M, Gutierrez-Uribe JA, Guajardo-Flores D (2017) Extraction of isorhamnetin conjugates from *Opuntia ficus-indica* (L.) Mill using supercritical fluids. J Supercrit Fluids 119: 58-63.

8. Ashtiani HRA, Bishe P, Lashgari N, Nilforoushzadeh MA, Zare S (2016) Liposomes in Cosmetics. J Skin Stem Cell 3(3): 65815.

9. Kapoor M, Lee SL, Tyner KM (2017) Liposomal Drug Product Development and Quality: Current US Experience and Perspective. AAPSJ 19(3): 632-641.

10. Euliss LE, DuPont JA, Gratton S, DeSimone J (2006) Imparting size, shape and composition control of materials for nanomedicine. Chem Soc Rev 35(11): 1095-1104.

11. Tsuji T, Morita SY, Ikeda Y, Terada T (2019) Enzymatic fluorometric assays for quantifying all major phospholipid classes in cells and intracellular organelles. Sci Rep 9(1): 8607.

12. Akbarzadeh A, Rezaei-Sadabady R, Davaran S, Joo W, Zarghami N, et al. (2013) Liposome: classification, preparation, and applications. Nanoscale Res Lett 8(1): 102.

13. Emami S, Azadmard-Damirchi S, Peighambardoust SH, Valizadeh H, Hesari J (2016) Liposomes as carrier vehicles for functional compounds in food sector. J Exp Nanosci 11(9): 737-759.

14. Jia Z, Dumont MJ, Orsat V (2016) Encapsulation of phenolic compounds present in plants using protein matrices. Food Biosci 15: 87-104.

15. D'Archivio M, Filesi C, Vari R, Scazzocchio B, Masella R (2010) Bioavailability of the Polyphenols: Status and Controversies. Int J Mol Sci 11(4): 1321-1342.

16. Shrivastava B, Gopaiah KV, Rao GS (2019) Lipid-polymer based nanoparticles as a new generation therapeutic delivery platform for ulcerative colitis *in vitro/in vivo* evaluation. Int J Innov Technol Expl Eng Sci 8(8): 3351-3359.

17. Shrivastava B, Gopaiah KV, Rao GS (2019) Lipid polymer based nano particles for the treatment of ulcerative colitis-review. Int I Res Anal Rev 6: 549-568.

18. Gopaiah MV (2019) Hydrotropic technique: a promising method to enhance aqueous solubility of nimesulide and to reduce difficulties in bioavailability. Asian J Pharm 12(4): S1456-S1472.

19. Gopaiah KV (2019) Validation Methods for the Simultanious Axitinib by a Reverse Phase HPLC. Lap lambert Academic Publishing, Germany, pp: 108.

20. Gopaiah KV (2019) Formulation and Development of Rosuvastatin Fast Dissolving Tablets. LAP Lambert-Publications, Germany, pp: 64.

21. Gopaiah KV (2019) Effect of analgesic activity in crude extract and isolated compounds of *Tecomaria capensis*. Int J Green Pharm 12(4): 322-328.

22. Gopaiah KV (2019) *In vitro and In vivo* anti-inflammatory potential of isolated compounds from ethyl acetate extracts of *Tecomaria capensis*. Int J Green Pharm 12(4): S1-57.

23. Gopaiah KV, Chowdar DP (2019) Validated Methods for the Quantification of Lacosamide Using RP-HPLC. Lap lambert Academic Publishing, Germany, pp: 88.

24. Gopaiah KV (2018) Design, formulation, and evaluation of sustained release tablets for antihyperlipidemic agent. Asian J Pharm 12(4): 312-319.

25. Rajeswari P, Kiranmai T, Manthrunaik D, Babu AVS, Kumar SM, et al. (2016) Formulation and characterization of colon specific drug delivery system of a matrix tablet. World Pharm 2(2): 330-348.

26. Chowdary KPR, Chandra DU, Mahesh N, Reddy TM, Gopaiah KV (2011) Enhancement of dissolution rate and formulation development of pioglitazone-ABCS class drug. Pharm Res 4: 3862-3863.

27. Gopaiah KV, Shristava B, Sharma PK, Rao GS (2004) Lipid polymer based nanparticles for the theropy of ulcerative colitis to improve the therapeutic efficiency. I Emerg Technol Innov Res 5(8): 1-12.

28. Junginger HE, Hofland HE, Bouwrtra JA (1991) Development of a topical anti-inflammatory gel from vitex negundo extract and evaluating it. Pharm Ztg 136: 9-24.

29. Tatipamula VB, Killari KN, Gopaiah KV, Alekhya Ketha A (2018) GC-MS Analysis of Ethanol Extract of *Taxithelium*

napalense (Schwaerg) Broth along with its alpha-Glucosidase Inhibitory Activity. IJPS 81(3): 569-574.

30. Tatipamula VB, Polimati H, Gopaiah KV, Babu AK, Vantaku S (2020) Bioactive Metabolites from Manglicolous Lichen Ramalina leiodea (Nyl.) Nyl. Indian Journal of Pharmaceutical Sciences 81(2): 379-384.

31. Gopaiah KV (2019) 1-8 Hydrotropic technique: A promising method to enhance aqueous solubility of nimesulid and to reduce difficulties in bioavailability. Asian journal of pharmaceutics 12(4).