Nanoencapsulation for Extraction and Release of Fragrance

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ABSTRACT: *This article discusses the synthesis of nanoparticles by inverse microemulsion polymerization and evaluates their potential to extract and release the fragrance linalyl acetate. The ability of the liposomes made from phosphatidyl choline and phosphatidic acid to extract organic molecules also is explored.*

During recent years, the significance of polymers and surfactants in the cosmetics and personal care industry has increased with their incorporation into a myriad of applications. Surfactants are used as emulsifiers, wetting agents, cleansers, foaming agents, solubilizers, conditioners and thickeners and to produce emolliency effects. Polymers, on the other hand, are employed to enhance system viscosity that in turn affects the rheology of the formulation. In skin care products, surfactants are used to prevent deposition of undesirable particles by emulsification, solubilization and dispersion.

Surfactants are amphiphilic moieties that form a link between two phases of markedly different polarity to reduce the surface tension at the interface. The mechanisms by which surfactants behave as cleansing agents previously have been described.[1]

Surfactants are classified as ionic or nonionic, depending on whether they ionize in aqueous media. Ionic surfactants are further classified as anionic, cationic and amphoteric compounds, depending on the charges on the surface-active portion of the molecule.

Apart from the mentioned functions, surfactants are used for the synthesis of microemulsions and nanoparticles by microemulsion method; microemulsions and nanoparticles are in turn used for flavors, fragrances and encapsulation of antimicrobial agents for such applications, and for antiperspirants and deodorants.

Encapsulation techniques are used in the food and cosmetic industries to control the release of entrapped materials and to protect against surrounding environments. Fragrance encapsulation and its controlled release play a key role in fragrance marketing; for example, fragrance samples incorporated as films or fine powders on magazine pages give consumers an opportunity to try the fragrance, enhancing its marketability. Encapsulation stabilizes the fragrance while controlled release prolongs its longevity.

Once the flavor or fragrance is encapsulated, controlled release is enacted by diffusion, pressure change, temperature sensitivity or other stimuli. The importance of encapsulation in food and cosmetics and various mechanisms of controlled release have been discussed in detail by Peppas.[2]

Microemulsions: A microemulsion is defined as a two-phase system consisting of two immiscible liquids, one of which is dispersed as finite globules in the other. The dispersed phase is referred to as the internal phase and the continuous phase is called the external phase. The most common types of emulsions include water as one of the phases and oil as the other. If the oil droplets are dispersed in a continuous aqueous phase, the emulsion is termed oil-in-water (o/w), whereas if oil forms the continuous phase, the emulsion is known as a water-in-oil emulsion (w/o). Figure 1 depicts an o/w microemulsion and a w/o, or inverse, microemulsion.

In microemulsions, the dispersed globules have radii of usually less than 10–75 nm. Surfactants promote emulsion stability by reducing the interfacial ten-

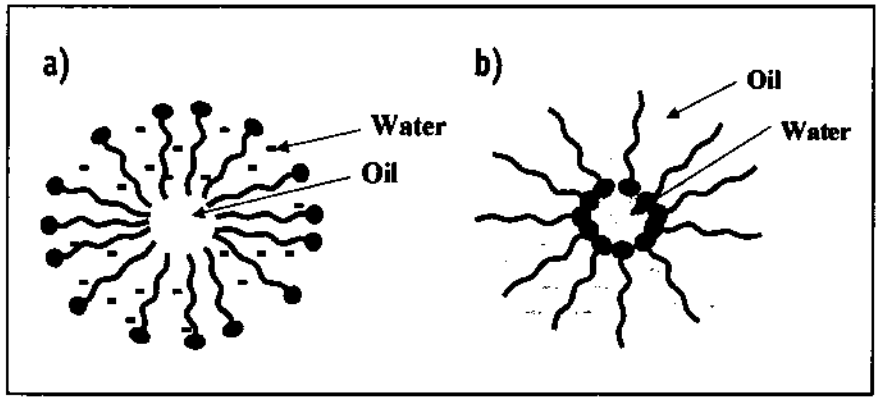

Figure 1. ***Depiction of a) water-in-oil (w/o) microemulsion and b) oil-in-water (o/w) microemulsion (inverse microemulsion)***

sion between the oil and water phases.[3] Microemulsions directly entrap flavors, fragrances and other attributes, or they act as nanoreactors for the synthesis of nanoparticles that are used for the encapsulation of such materials.

In cosmetic formulations, o/w microemulsions find much broader applications than w/o microemulsions. One important area of application of o/w microemulsions is the solubilization of fragrances and flavor oils in products such as cologne, after shave, skin freshener, hair tonic and mouthwash. Though the surfactants are effective in solubilizing oily flavor and fragrances, it has been demonstrated that the odor intensity decreases with an increase in the surfactant concentration in the formulation.[4] Moreover, surfactants associated with microemulsion formulations have toxic and irritating effects on the skin and can penetrate the skin barrier—for example, diethanolamides used as surfactants for cosmetic formulations are carcinogenic in nature and can penetrate the skin. An alternative solution is the use of nanoparticles and liposomes for encapsulation of personal care products.

Liposomes: *Liposomes*, or (phospho)lipid vesicles, are self-assembled colloidal particles. They are spherical vehicles of phospholipids with an aqueous cavity that engulfs water-soluble actives (see **Figure 2**).

Liposomes were introduced as drug-delivery vehicles in the 1970s. Current industrial applications of liposomes are based on their colloidal properties including size, microencapsulation, membrane mechanical strength and surface properties. Among the various delivery systems or carriers, liposomes have been the most widely investigated and marketed by the cosmetic industry because they are benign, biocompatible and can encapsulate a wide variety of attributes.

Liposome applications in cosmetics are based on their ability to solubilize hydrophobic molecules in natural lipid-water systems, act as a slow release reservoir, and possibly enhance penetration through mucosal membranes. They have been incorporated into several hundred products on the market including sunscreen lotion, skin creams and perfumes. The first cosmetic applications of liposomes were as moisturizing agents for the hydration of the skin. Cosmetic applications of liposomes have been discussed in detail by Benita et al.[5] Liposomes are highly biocompatible and reduce irritation but they are less stable than nanoparticles.

Nanoparticles

A *nanoparticle* is a reservoir that encapsulates an active substance in order to protect and isolate it from the

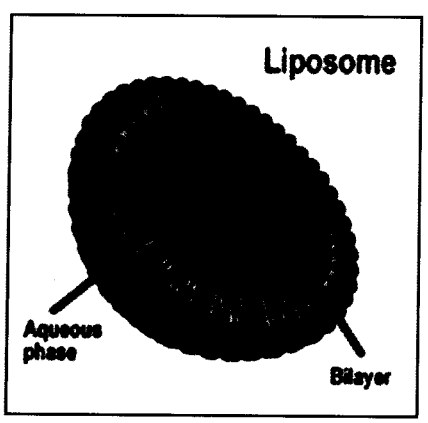

Figure 2. ***Spherical vesicles of phospholipids engulf water-soluble actives.***

surrounding environment and to adjust its properties in accordance with specified requirements. Nanoparticles are used widely for preparations containing drugs, vitamins, steroids, proteins, enzymes, flavors and fragrances. The primary objective of nanoparticles is to provide formulations with prolonged activity, protection against adverse conditions and controlled release of the active ingredient.

Nanoparticles are divided into two main categories: nanospheres and nanocapsules. Nanospheres are nanoscale porous particles formed by crosslinking the polymer chains whereas nanocapsules are hollow structures formed from block copolymers.

Nanospheres are polymer matrices in which the active material is dissolved or dispersed. In the case of nanocapsules, a polymer wall entraps an oily reservoir in which the active material is dissolved.

In general, nanoparticles refer mainly to nanospheres in the literature. Nanoparticles, owing to their submicron size, are well-dispersed into cosmetic products. They also can encapsulate a great amount of fragrance because of their large surface area.

A *microemulsion* is defined as a two-phase system consisting of two immiscible liquids, one of which is dispersed as finite globules in the other.

Poly(acrylic acid) for Extraction and Release of Fragrance

Poly(acrylic acid) (PAA) and hydrophobically modified PAA nanoparticles were synthesized by reverse microemulsion method. The potential of these nanoparticles to extract and release the fragrance linalyl acetate was evaluated.

Poly(acrylic acid) (PAA) is a biodegradable, biocompatible, mucoadhesive polymer and has found applications as a drug carrier.[6,7] Though a significant amount of work has been carried out on the drug delivery applications of PAA, little work has explored its potential as a fragrance carrier. The bio-friendly nature of PAA in nanoparticle form prompted the investigation of its ability to extract

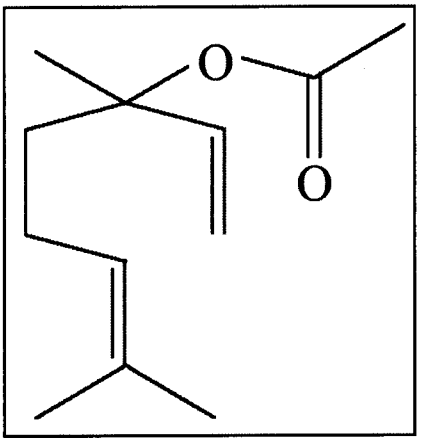

Figure 3. ***Linalyl acetate structure***

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fragrance. The fragrance linalyl acetate was selected for this study since it is one of the most extensively used fragrance ingredients in decorative cosmetics, deodorant soaps, shampoos and detergents. Its worldwide use is approximately >1000 metric tons per year.[8] Letizia et al. have presented a toxicologic and dermatologic review of its use as a fragrance ingredient.[8] The structure of the molecule is shown in **Figure 3**.

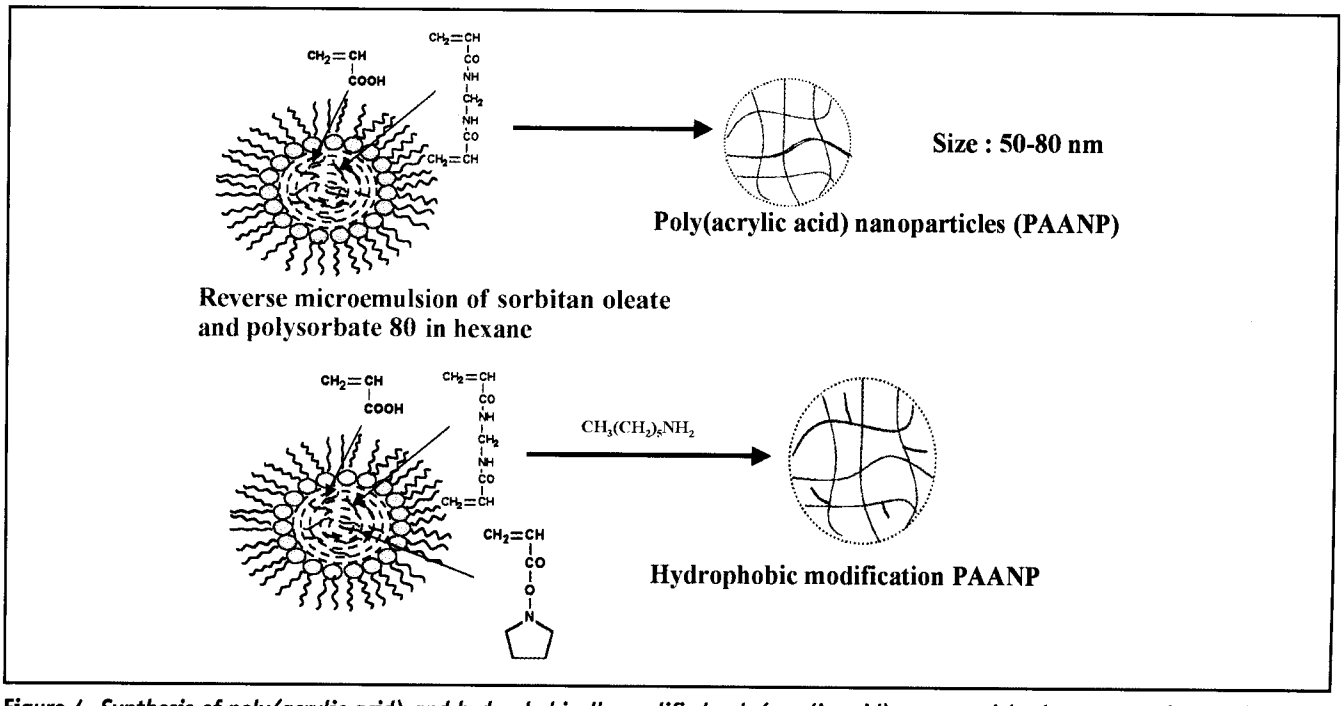

Figure 4. ***Synthesis of poly(acrylic acid) and hydrophobically modified poly(acrylic acid) nanoparticles by reverse microemulsion polymerization method***

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Materials and Methods

Nanoparticles were prepared inside the inverse microemulsion formed by sorbitan oleate and polysorbate 80 in presence of hexane and water. N,N'-methylene bisacrylamide was used as the cross-linking agent and the reaction was initiated by γ radiation. Hydrophobic modification was carried out by copolymerizing N-acryloxy-succinimide material into PAA and then substituting it by hexylamine into the nanogels structure. The reaction scheme is shown in **Figure 4**.

The nanoparticles were 50–80 nm in size. Poly(acrylic acid) and hydrophobically modified poly(acrylic acid) nanoparticles prepared by the above method were dispersed in methanol solution of linalyl acetate (PAA: linalyl acetate = 10:1wt/wt) and the potential of these nanoparticles to extract linalyl acetate from methanol was evaluated. PAA nanoparticles were filtered out at different time intervals and the concentration of residual linalyl acetate was determined using high performance liquid chromatography (HPLC).

Hexylamine modified nanoparticles were found to extract more linalyl acetate than the unmodified nanoparticles (**Figure 5**). This enhanced extraction in the case of hydrophobically modified nanoparticles has been attributed to the favorable hydrophobic interaction between the hexylamine-modified nanoparticles and the hydrophobic fragrance molecules.

The release of fragrance in aqueous medium was found to be pH-dependent (**Figure 6**).

In case of the modified and unmodified nanoparticles, release of fragrance was more pronounced in neutral (pH 7) and alkaline (pH 9) conditions than in acidic (pH 4) conditions. In neutral and alkaline media, the nanoparticles swell because of the ionization of the carboxylic groups attached to the polymer backbone and release the entrapped fragrance.

PAA nanoparticles could potentially be dispersed in a solution of deodorant within a pH range of 7-9, causing nanoparticles to swell and thus allowing deodorant to penetrate inside.

Encapsulation with Liposomes

Liposomes are vehicles similar to nanogels with hydrophobic domains but with different permeation properties. They control the uptake and release of fragrance by manipulating the components within the structure of the liposomes. Apart from nanogels, the potential of liposomes to extract organic materials such as amitriptyline also was evaluated. The liposomes used for the study were made from 1:1 phosphatidyl choline and phosphatic acid. The drug concentration in the lipid bilayers after interaction of the liposomes with amitriptyline was determined. The result is shown in **Figure 7**.

In the absence of salt, the drug concentration in the lipid bilayers

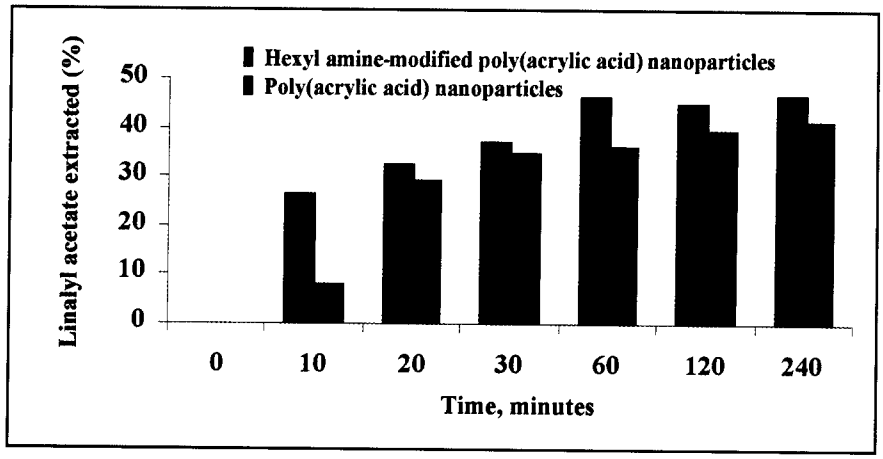

Figure 5. *Extraction of linalyl acetate by poly(acrylic acid) and hexylamine-modified poly(acrylic acid) nanoparticles*

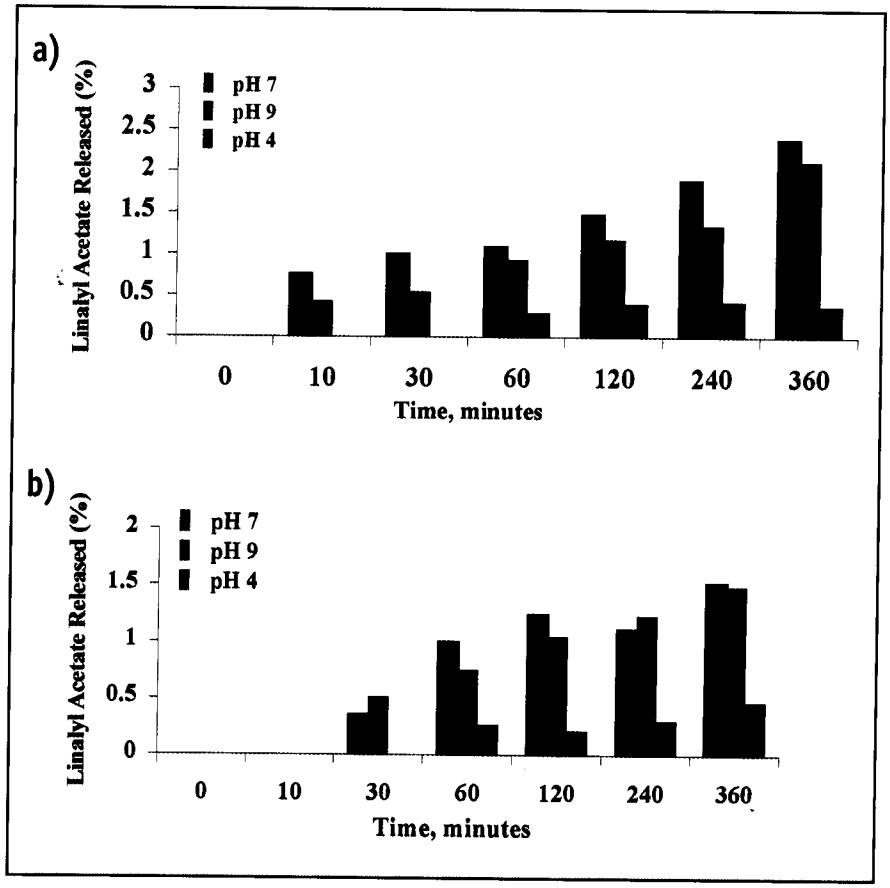

Figure 6. *Release of linalyl acetate by a) poly(acrylic acid) nanoparticles and b) hexylamine modified poly(acrylic acid) nanoparticles as the function of pH of the dispersion medium*

increased linearly with an increase in the drug concentration. In water, the surface charge of the lipsomes is highly negative due to the presence of the anionic groups on both phosphatidic acid and phosphatidyl choline. This favors electrostatic interactions between the liposomes and the cationic drug molecule as shown in **Figure 8**.

In the presence of a phosphate buffer (ionic strength 0.1 M), however, a significant decrease in the partitioning of the drug into the lipid bilayers was observed because of the decrease in electrostatic interaction. In the phosphate buffer, maximum drug partitioning into the liposomes was observed at 6 mM drug concentration. Complete destruction of the liposome structure was detected on further increase in drug concentration due to the decrease in the electrostatic effect. In the presence of oppositely charged ions, the electrostatic attraction between bulky head groups of drug molecules are neutralized. Therefore, these molecules could easily form mixed micelle structures in the presence of phopholipid molecules.

Summary

Novel poly(acrylic acid) nanoparticles with a narrow size distribution were synthesized using inverse microemulsion polymerization technique and were hydrophobically modified by attaching a hexyl group from hexylamine to the nanoparticle backbone. By introducing functional groups into the nanoparticles, the nanoenvironment of the nanoparticles was modified with a significant impact on the interaction between nanogels and tested fragrance molecule.

Modified nanoparticles showed enhancement in fragrance binding compared to the unmodified nanogels in methanol. They showed pH-sensitive fragrance release, which was better at pH levels 7 and 9 than in pH 4. Liposomes made of phosphatidyl choline and phosphatic acid also extracted amitriptyline in water, indicating that they have the potential to extract other organic as well as inorganic attributes whose polarity is comparable with amitriptyline. Thus nanoparticles and liposomes with appropriate modification offer a promising route for fragrance extraction and release. However, further experiments need to be performed in order to test their efficacy before they are used to encapsulate other actives.

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References

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1. P Somasundaran, L Zhang and A Lou, *Cosmetics & Toiletries* 116 (7) 53 (Jul 2001)
2. LB Peppas, Polymeric delivery systems: Properties and applications, MA El-Nakoly, DM Piatt and BA Charpentier, eds, *ACS Symposium Series* 520 45 (1996)
3. JM Blakeway, P. Bourdon, M. Seu, *Int J Cosmet Sci* 1 1(1979)
4. M Seiller, M-C Martini, S Benita, Microencapsulation: Methods and industrial applications, S Benita, ed, New York: Marcel Dekker Inc 587 (1996)
5. *http://saints.css.edu/bio/schroeder/liposome.gif*
6. B Kriwer, E Walter, T Kissel, *J of Controlled Release* 56 149 (1998)
7. N Peppas, *Hydrogels in Medicine and Pharmacy*: CRC Press: Boca Raton, FL (1986)
8. CS Leitizia, J Cocchiara and J Lalko, AM Api, Food and Chemical Toxicology 41 965 (2003) C&T

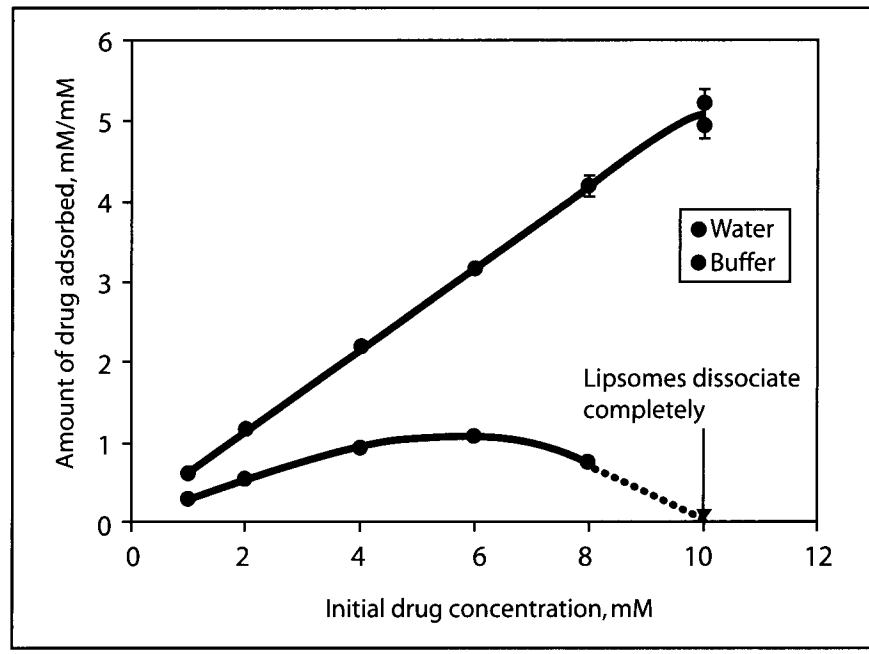

Figure 7. ***Drug concentration in the lipid bilayers after interaction of liposomes with amitriptyline***

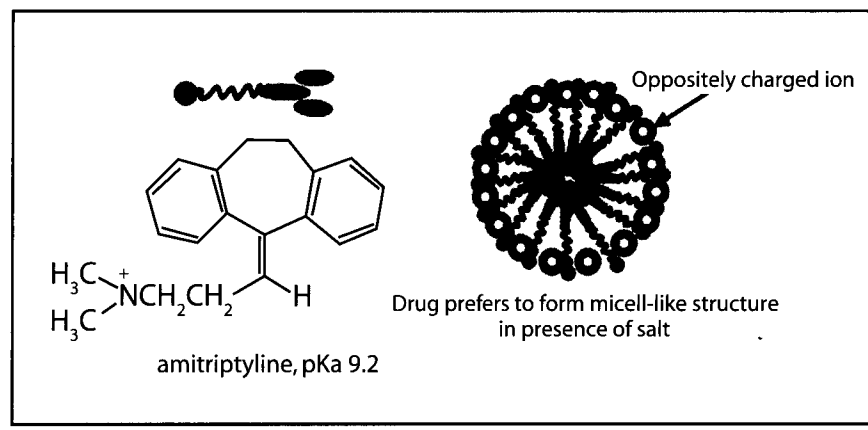

Figure 8. ***Schematic representation of effects of oppositely charged ions in micelle formation of amitriptyline***