



CYCLODEXTRINS “World’s Smallest Beauty Cases”

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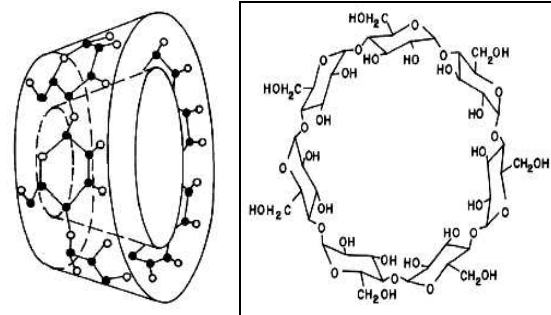
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Abstract: In today’s beauty conscious world especially showbiz where people are disposed to pay any hefty amount for beautification and body care, cyclodextrins have carved a niche for them in cosmetic industry. The most common application of cyclodextrins in the formulation development is to enhance the solubility, stability, safety and bioavailability of drug molecules, besides key importance in cosmetic industry. In cosmetic industry the Cyclodextrins (CD’s) are known as “world’s smallest beauty cases” because an anti-ageing active ingredient RETINOL only in 0.1% in anti-wrinkle creams can cause skin irritations, but when formulated with CDs as an inclusion complex much higher concentrations of active ingredient can be added to cosmetics without causing skin irritation and the retinol is released gradually. Since the CD molecule encases the RETINOL, CDs are therefore termed as WORLD’S SMALLEST BEAUTY CASES [1,2,15]. Cyclodextrins are non-toxic polysaccharides which belong to the family of cyclic oligosaccharides composed of α -(1, 4) linked glucopyranose subunits and are useful molecular chelating agents. CD’s possess cage like or toroidal structure which can entrap molecules having poor solubility and thereby enhances their solubility besides masking the obnoxious taste and odour. These compounds having supramolecular structures carry out chemical reactions that involve intramolecular interactions where covalent bonds are not formed. As they form inclusion complexes, the properties of guest molecules can be altered to a large extent. Their importance in cosmetology ranges from fairness creams to anti-wrinkle preparations and never ending list of cosmetics and toiletries up to the latest Glutathione injections used for enhancing fairness. The slow release of fragrances in Talcum powders and Perfumes is achieved by the use of cyclodextrins. Apart from stabilising a sensitive drug molecule against light or oxygen, CD’S can modify the chemical reactivity of guest molecules. This article highlights the potential use of cyclodextrins in cosmetic formulations with more emphasis on recent developments.

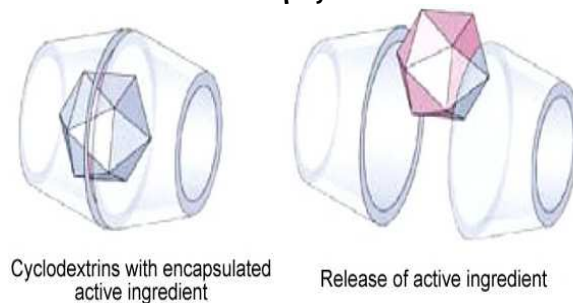
Keywords: Cyclodextrin, Supramolecular structures, Bioavailability, Polysaccharides, Glutathione, Retinol.

INTRODUCTION

Cyclodextrins are of immense interest in the Pharmaceutical field due to its potential to entrap entirely or at least partially a wide variety of drug molecules, both branched as well as unbranched. It is a toroidal shape structure [3,4,5]. A French scientist Villiers, first described a crystalline substance isolated from bacterial (*Bacillus macerans*) by digestion of starch [6,7]. The hydrophilic external phase and hydrophobic inner surface makes them the most important single organic compound, which is capable of forming more soluble and stable non covalent bonds with host-guest system [8,9,10]. Cyclodextrins are a group of structurally related natural products and are also known as cycloamylosis or as ‘Schardinger dextrins’. The CD’s are water soluble, non-reducing macrocyclic polymers containing glucose molecules joined by α 1, 4- linkages. The most common of these compounds are the β and γ CD’s formed by 6, 7 and 8 glucose units respectively. The ring shaped molecules encloses a cavity of about 6, 8 and 10 Å in diameter for the α , β and γ CD’s respectively [11,12,13,14].



Chemical structure of β cyclodextrin molecule [15]



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Advantages in Cosmetic Formulations:

Protection of the guest molecule: ^[16,17,18,19,20] CD's provide protection against decomposition reactions induced by light, heat, oxidation, hydrolysis, chemical reactions with other organic compounds, or loss by evaporation) for example Hydroquinone is a skin bleaching agent used for skin whitening. In aqueous formulations hydroquinone is stable only in a limited-pH range. Therefore stabilizers are normally used. Due to the prevention of the oxidation of hydroquinone the cyclodextrin complexes have a greater stability. They also show greater depigmentation effect than the hydroquinone itself (see table below).

Solubilisation of the guest molecule:^[21,22,23,24,1]

(increasing solubility, increasing rate of solubilisation avoidance of organic solvents, change of viscosity). A large number of cosmetic components are nearly insoluble in water. few examples are vegetable oils, hydrocarbons higher fatty acids and their esters, vitamins, hormones, antiphlogistics and preservatives All these chemical substances are able to form inclusion complexes with cyclodextrins and cyclodextrin complexes are more soluble compared to pure compounds This effect is generally used for the formulation of cosmetics ^[21].Matsuda, Ito, Taki and Uejima.1983].

Cosmetic Components Like Vegetable Oils, Hydrocarbons, Higher Fatty Acids & their Esters, Vitamins Hormones, Antiphlogistics & Preservatives	Cosmetic Ingredients/Component	Use	Marketed Preparation
Salicylic acid	Keratolytic and antibacterial	Enhances the solubility of the acid or its derivatives in aqueous solution possibly reducing irritant action of acids on skin and thereby enhancing the disinfectant bacteriostatic and Keratolytic properties.	Bioclin Sebocare Impure skin cream (Gannasini) ^R
Triclosan	Personal Care product topical antiseptic and disinfectant in mouthwashes.	CD complexation is soluble in water giving a clear solution.	
Menthol	Cooling agent in cosmetics	Solubility enhancement in aqueous form thereby avoiding the use of alcohol. U.V light and oxygen initiate chemical reactions of retinol. During oxidation some peroxidic toxic intermediates are formed and CD complexation prevents such type of oxidation. Also solubility enhancement of retinol. Just recently formation of complexes with γ -cyclodextrin.	Lipo chemicals formulations.
Retinol	Topical anti-ageing, reduces wrinkles and supports the restoration of U.V damaged tissues.		Eucerin Vital Retinol ^R (Beiersdorf), Nutrients and Anti-ageing (Efal) and Dexol ^(R) (Collaborative laboratories)
Topical skin fat removal formulations	Skin cleaning	Able to complex with CDs and dissolves skin fat	(Gesichtnonic)

Elimination of undesired odours or tastes and hygroscopicity: ^[25,26,27,28] Dihydroxyacetones used as tanning agents are not stable in aqueous solution. More importantly their unpleasant odour is difficult to mask by perfumes. This odour vanishes by using the cyclodextrin complex. The slow release of dihydroxyacetone from the complex results in a more uniform tanning of the skin. Another example is of glutathione. Glutathione shows various physiological activities. For example, it inhibits melanin pigment formation. Thus it may be used for skin whitening and improving the texture of skin. But unfortunately glutathione generates an offensive odour in cosmetic formulations, here the complexation of glutathione with cyclodextrin makes it free of odour and the complex has the same unchanged effect.

Improvement of handling of Liquid or oily substances as powders:^[16,29,30,31] The oily form of a tocopherol is an antioxidant and is used in personal care products to protect the surface of stratum

corneum from damage caused by free radicals. As a cyclodextrin complex it is not soluble in water or oil. It should be used as a powder or suspended in lotions and creams. Therefore formation of complexes with cyclodextrins enhances the stability of tocopherol.

Not a nutrient medium for microorganisms unlike starch:

In contrast to starch cyclodextrins and their derivatives are not a medium for microorganisms. As a result the use of preservatives in formulations can be reduced.

Protection Of Guest Molecule: [17,18,19, 20].

PREPARATION	USE	FUNCTION OF CD	MARKETED PREPARATIONS
Tea tree oil	Antimicrobial	CD complexation protects from light and oxygen.	EpicutinTTR (Chem Laboratories)
Hydroquinone	Skin whitening	Prevention of oxidation and enhancing depigmentation effect of HQ.	
Kojic acid	Whitening agent in cosmetics	Protection against light and heat as Kojic acid is very labile.	
Peroxyacetic acid	Skin lightening	CD complexes form solid complexes with α and β CD which act as mild oxidants with disinfectant properties.	

Protection Against Loss By Evaporation: [32,33,34]

PREPARATION	USE	FUNCTION OF CD	MARKETED PREPARATIONS
Perfumes (citral)	Fragrances in long acting perfumes.	Stabilised against evaporation as CD complexes,	Vivace ^R (Shiseido)

Solubilisation Of Guest Molecules: [21,22,23,1,2]

Elimination Of Undesired Odors: [25,26, 27,28]

PREPARATION	USE	FUNCTION OF CD	MARKETED PREPARATION
Dihydroxyacetone	Tanning Agent	Unpleasant odour of dihydroxy acetone is difficult to mask by the use of perfumes. This odour vanishes using the CD complex and slow release of dihydroxy acetone causes uniform tanning. Masks the offensive odour of glutathione and makes it odourless and has same effect as glutathione. Mercapto compounds in these lotions have extremely unpleasant odour, which is masked by CDs. Unpleasant odour is masked by complexation with CDs and antiphlogistic activity of chamomile remains unaffected. CD's and mixtures can be used in deo sticks.	Ultra sun Selftan ^R (Ultrasun).Self Action Super Tan for (Estee Lauder)
Glutathione	Inhibits melanin pigment formation therefore used for skin whitening and skin improving effects.		Tatiomax Gold Reduced Glutathione with Collagen IM/IV for injection
Hair waving lotions	Used for straightening and curling of hair.		
Chamomile extracts or oil	Antiphlogistics, bacteriostatic wound healing effect.		
Deodorant (farnesol complexes)	Odour control by microbial degradation of sweat.		

Improvement Of Handling Of Liquid Or Oily Substances, Powders: ^[16, 29, 30, 31]

PREPARATION	USE	FUNCTION OF CD	MARKETED PREPARATION
Alpha-tocopherol	Antioxidant used in personal care products to protect the surface of the stratum corneum from damage caused by free radicals.	The formation of complexes – with CD serves to enhance the stability of tocopherol.	
Octylmethoxy cinnamate (oil-soluble sunscreen)		CD's complexes of octyl-methoxy cinnamate release it slowly and long lasting protection of the skin.	Lipo-Chemicals (Inc)

Few preparations of Cosmetics: ^[37-53]

Formula 1.

- A. Glyceryl –polymethacrylate -**20.0%**
- B. phenoxyethanol and methyl paraben and butyl paraben, ethyl paraben, propyl paraben-**0.2%**
- C. Imidazolidinyl urea -**0.3%**
- D. Hydroxy propyl –cyclodextrin ,musk oil, rose oil (polyunsaturated fatty acids from musk rose oil cyclostern complex).**2.0%**
- E. Hydroxy propyl cyclodextrin and retinyl acetate (vitamin A acetate cyclosystem complex).**2.0%**
- F. water -**q.s**

Total -**100.**

Procedure: Dissolve B,C,D and E in cold water F. Add A.Mix untill you obtain a homogenous gel.

Formula.2:

Absorbent foot powder .

- A. Micronised Talc-**70.0%**
- B. Rice Starch Powder -**20.0%**
- C. Cyclodextrin and fragrance (fragrance cyclosystem complex) -**6.0%**
- D. β - Cyclodextrin -**100.0**

Procedure :Mix A, B,C and D untill you obtain a homogenous powder.

Formula.3:

Spray Deodorant

- A. Triclosan-**0.30%**
- B. Alcohol and iceland moss extract -**2.0%**
- C. Ethyl Alcohol – **50.0%**
- D. Cyclodextrin (α -CD)-**0.30%**
- E. Cyclodextrin (β -CD)-**0.40%**
- F. Dimethicone -**0.50%**
- G. Cyclodextrin and hydroxy proline and sodium PCA and hydrolysed collagen and propylene glycol. (Moisturising factor cyclosystem complex)-**2.0%**
- H. Water -**43.70.**
- I. Fragrance-**1.00%**

Total – **100.**

Procedure:

Dissolve A-G in cold water H. Mix untill homogenous . Add fragrance I and mix.

Future prospects of Cyclodextrins: ^[52, 53]

The future of Cyclodextrins in the Pharmaceutical and cosmetic industry seems to be bright ranging from drug delivery to role in treatment of HIV infections, in health care and space science to cosmetics. New uses of cyclodextrins are likely to be explored as the properties of cyclodextrins are expanded and the number of commercialized and FDA-approved variants increases. Presently only conventional formulations such as tablets, capsules, solutions, ointment and intravenous solutions have been commercialized using Cyclodextrins. Nowadays, Cyclodextrins are extensively being studied for their application in Novel drug delivery such as Nanoparticles, Liposome, Microspheres and targeted drug delivery and they become commercially available in future. Gene therapy also continues to generate interest with cyclodextrins. With the difficulty in viral gene delivery, non-viral methods are being further explored. Polycation Cyclodextrins have unique properties that could be useful in the non-viral delivery of nucleic acids. Showing promise for gene delivery in animals, although their utility in humans remains to be proven.

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