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A Review On: Cyclodextrins

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ABSTRACT

Cyclodextrins are non-toxic cyclic polysaccharides. They form inclusion complexes with numerous organic molecules. The physical and chemical properties of the guest molecules change due to complex formation. Cyclodextrins (CDs) are chemically cyclic oligosaccharides which have been recognized as useful pharmaceutical excipients. Cyclodextrins are versatile pharmaceutical excipients used to enhance the solubility, stability, safety and bioavailability of drug. Besides, being used to reduce gastrointestinal drug irritation, convert liquid drug into microcrystalline or amorphous powder, and prevent drug-drug and drug-excipients interactions. The solubility of slightly soluble molecules may be increased by cyclodextrin inclusion complex. As a result of molecular complexation phenomena cyclodextrins are widely used in many industrial products, technologies and analytical methods.

Keywords: Cyclodextrins, Solubility, Complexation, Applications

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INTRODUCTION

Cyclodextrins (CDs)are cyclic oligosaccharides containing of six α-cyclodextrins, seven β-cyclodextrins, eight γ-cyclodextrins or more glucopyranose units linked by α-(1,4) bonds. They are also known as cycloamyloses, cyclomaltoses and Schardinger dextrins. Cyclodextrins has hydrophilic outer surface and lipophilic central cavity. They are able to form water soluble inclusion complexes with many lipophilic water insoluble drugs. Due to this, cyclodextrins are useful molecular chelating agents. The solubility of slightly soluble molecule increases in a cyclodextrin complex. The cyclodextrin have wide range of application in different areas of drug delivery and pharmaceutical industry due to their complexation ability and other versatile characteristics. Cyclodextrins influences most important drug properties in formulation such as solubility, dissolution, bioavailability, drug safety and drug stability.[1, 2]

History

Cyclodextrins (CDs) have been known for over 100 years as excipients of considerable important in the pharmaceutical field. [3, 4, and 5] The first reference to cyclodextrin was published in 1891.[6] In 1891, a French scientist Villiers first described cyclodextrins as a crystalline substances isolated from bacteria (*Bacillus Macerans*) by digestion of starch.[7, 8] The substance was a dextrin and Villiers named it as "Cellulosine". Some year later Schardinger also observed the formation of cyclodextrins.[9] About 15 years later, an Austrian microbiologist, Franz Schardinger, described two crystalline compounds α-dextrin and β-dextrin which he had isolated from a bacterial digest of potato starch. Schardinger identified β-dextrin as Villiers ''Cellulosine". [10]

Freudenberg continued in studying these compounds obtained from starch.[11] He called them Schardinger dextrins. Beginning at that time, they were also called "Cyclodextrins" i.e. α-cyclodextrins (α-CD) and β-cyclodextrin (β-CD) or less commonly cyclomaltodextrins (i.e. cyclomaltohexaose and cyclomaltoheptaose) or cycloamyloses (i.e. cyclohexaamylose and cycloheptaamylose). γ-cyclodextrin (γ-CD; cyclomaltooctaose or cycloactaamylose) was first described in 1935 by Freudenberg and Jacobi.[12] At that time, structure of these compounds were still uncertain, but in 1942, the structure of α and β-cyclodextrin were determined by x-ray crystallography.[13] In 1948, the x-ray structure of γ cyclodextrin followed and it was recognized that cyclodextrins can form inclusion complex. In the beginning of the 1950s, French and Cramer[14] began to work together on the enzymatic production of cyclodextrins on fractionating

them to pure components and on characterizing their true chemical and physical properties. Freudenberg, Cramer and Plieninger obtained a patent in 1953.[15]

The first fundamental review on cyclodextrins was published in 1957 by French. It was followed in 1965 by a monograph by Thema and Stewart and in 1968 by Caesar. In 1970, cyclodextrin was only available as a rare fine chemical at a price of about US$ 2000 per Kg. Today the annual cyclodextrin production is close to 10,000 tones and the bulk price has lowered to about US$ 5 per kg. However, in 1980, Saenger published a review article about cyclodextrin [s] [16] in which he mentioned some industrial applications. The First International Cyclodextrin Symposium Organized by Szejtli took place in Budapest in 1981.[17] One year later the first cyclodextrin book written by Szejtli was published. Since then an increasing interest in cyclodextrins and their possible applications has existed.[18] In they are following, these discoveries, large ring cyclodextrins (L.R-cyclodextrins) were discovered.[19] Presently only α-cyclodextrin, β-cyclodextrin and γ-cyclodextrin, as well as some of their derivatives have advanced to the market.

Structure and Physicochemical Properties Of Cyclodextrins

Cyclodextrins are cyclic (α-1, 4) linked oligosaccharides of α-D-glucopyranose containing a relatively hydrophobic central cavity. Due to their chain formation of glycopyranose units, cyclodextrins are cone or toroidal shaped rather than perfectly cylindrical molecule. Primary hydroxyl groups are located on the narrow side of the torus while the secondary hydroxyl groups are located on the wider edge. The central cavity is lined by the skeletal carbon and ethereal oxygen's which give it a lipophilic character. The natural products consist of mixture of the various cyclodexrin mainly α-cyclodextrin, β-cyclodextrin, and γ-cyclodextrin containing six, seven and eight glycopyranose units respectively. These naturally occurring products have limited aqueous solubility due to the strong intermolecular hydrogen bonding in the crystal state. Substitution of the H-bonds forming OH groups has improved their solubility. [20] The hydrogen bond strengths are α-cyclodextrin < β-cyclodextrin < γ-cyclodextrin. β -cyclodextrin the most common natural cyclodextrins has 21 hydroxyl groups that are 7 primary and 14 secondary hydroxyls. [21]

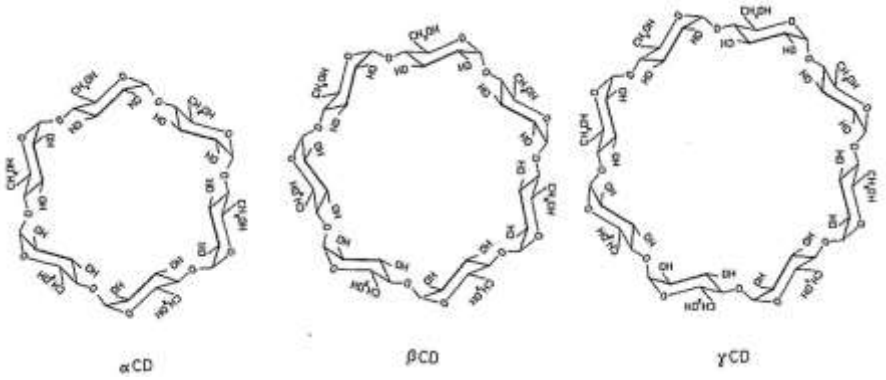

Figure 1: Chemical structure of α, β, γ cyclodextrins

All three cyclodextrins have similar structure (i.e., bond length and orientation) apart from the structural necessities of accommodating a different number of glucose residues.

The typical structure of cyclodextrins confers upon these molecules. A wide range of chemical properties markedly different those exhibited by non cyclic carbohydrates in the same molecular weight range. This include-

• Cyclodextrins are water soluble.

• The microenvironment in their cavity is relatively non polar and lipophilic.

• The ring structure has neither a reducing nor non reducing end group.

• They are not decomposed by alkali.

•They are rather resistant to hydrolysis by (organic) acids and many common α-amylases and completely resistant to yeast fermentation and β-amylases.

• They exhibit enhanced thermal stability with a decomposition temperature approaching 300^0C.

Cyclodextrins containing nine, ten, eleven, twelve and thirteen glucopyranose units, which designated as δ, ε, γ, η and θ respectively.[22] (Table 1) [23]

Table 1: The chemical and physical properties of three most common cyclodextrins are given in table.

Sr. No	Properties	α-CDs	β-CDs	γ-CDs
1	No of glucopyranose units	6	7	8
2	Molecular weight (gm/mol)	972	1135	1297
3	Solubility in water at 25˚C (%w/v)	14.5	1.85	23.2
4	Outer diameter (A˚)	14.6	15.4	17.5
5	Cavity diameter (A˚)	4.7-5.3	6.0-6.5	7.5-8.3
6	Height of torus (A˚)	7.9	7.9	7.9
7	Cavity volume (A˚³)	174	262	427
8	Surface tension (N/m)	71	71	71
9	Water of crystallization (W/V %)	10	13-15	8-18
10	Melting point (˚C)	250-260 ˚C	255-265 ˚C	240-245 ˚C

Studies of cyclodextrins in solution supported by a large number of crystal structure studies. Cyclodextrins crystallize in two main types of packing, channel structure and cage structure, depending on the type of cyclodextrins and guest compound. Apart from these naturally occurring cyclodextrins, many cyclodextrin derivatives have been synthesized. These derivatives usually are produced by amination, esterification or etherification of primary and secondary hydroxyl groups of the cyclodextrins. [24] Then the natural and chemical modified cyclodextrins have been extensively utilized to improve various drug properties, such as solubility, dissolution and rate stability or bioavailability. [25]

Cyclodextrins are the most widely used molecules that from host/guest type inclusion complexes. This is dynamic process whereby the guest molecule continuously associates and dissociates from the host cyclodextrins. Cyclodextrins are insoluble in most organic solvent; they are soluble in some polar, aprotic solvents. The solubility of cyclodextrin is higher in some organic solvents than in water. Complexation may not occur readily in non- aqueous solvents because of the increased affinity of the guest for the solvents compared to its affinity for water. Cyclodextrin derivatives of industrial interest include the hydroxypropyl derivatives of β and γ cyclodextrin, the randomly methylated β-cyclodextrin, sulfo butyl ether β-cyclodextrin, the acetylated β and γ cyclodextrin, and the Saccharide conjugated cyclodextrins. [26]

METHODS OF COMPLEXATION TECHNIQUES

Following techniques are used to form complexes with cyclodextrins.

Physical blending/Grinding method

Cyclodextrin- drug inclusion complexes can be prepared by simple grinding or by trituration method. On small scale grinding or trituration can be carried out by mortar and pestle. While on large scale inclusion complexes can be prepared by extensive blending of the drug with cyclodextrin in a rapid mass granulator for 30 minutes. Sapkal (Sapkal N P, et al 2007) had evaluated some methods for preparing Gliclazide-β-cyclodextrin inclusion complexes. [27]

Solid dispersion/ Co-evaporated dispersion

The drug is dissolved in ethanol and cyclodextrin is either dissolved in alcoholic solution or dissolved separately in water or other suitable medium. The cyclodextrin solution is then added to the drug solution or vice-versa and stirred to attain equilibrium. The resulting solution is evaporated to dryness preferably under vacuum. [28]

Kneading method

Paste of cyclodextrin is prepared with small amount of the solvent and in that drug is added slowly. Slurry is kneaded for 45 minutes. During this kneading appropriate quantity of solvent is

added in slurry to maintain consistency. Further product is dried at 40^0 C for 48 hours. Fernandes (Fernandes C M et. al 2002) had studied physicochemical characterization and in vitro dissolution behavior of Nicardipine–cyclodextrins inclusion compounds. [29]

Co-precipitation method

Drug is dissolved in solvent at room temperature and cyclodextrin in distilled water. The mixture is stirred at room temperature for 1 hour, and then slowly evaporated on boiling water bath. The inclusion complex precipitated as a crystalline powder is pulverized and passed through sieve No. 80 and stored in a desiccator till free from any traces of the organic solvent. Sreenivasa Rao K **(**Sreenivasa Rao K et. al 2012**)** had studied **c**yclodextrin inclusion complexes of water insoluble drug-Glimipiride. [30]

Spray drying

The drug and cyclodextrin is dissolved in solvent and distilled water separately with the help of a magnetic stirrer. Both the solutions are mixed slowly and drop wise together on a magnetic stirrer for 30 min to attain equilibrium following which the solvent is removed by spray drying. Shirala shetti (Shirala shetti et. al. 2010) had studied Simvastatin cyclodextrin inclusion complexes. [31]

Neutralization method

Drug is dissolved in 1 N NaOH solution followed by the addition of cyclodextrin. The mixture is placed on a magnetic stirrer and stirred until dissolved. Equal amounts of 1 N HCl is added drop-wise and the solution is stirred for 2 hours with magnetic stirrer. The precipitated product is filtered off under vacuum and dried at room temperature. Abou- Auda (Abou- Auda H.S. et.al 2006) studied Gliclazide- β cyclodextrin complexes. [32]

Lyophilization/ Freeze drying method

In this technique, the solvent system from the solution is eliminated through a primary freezing and subsequent drying of the solution containing both drug and cyclodextrin at reduced pressure. Nicolescu (Nicolescu C et. al 2010) had studied inclusion complexes between repaglinide and β -cyclodextrin, 2- hydroxypropyl – β- cyclodextrin and randomly methylated β- cyclodextrin. [33]

Microwave irradiation method

This technique involves the microwave irradiation reaction between drug and complexing agent using a microwave oven. The drug and cyclodextrin in definite molar ratio are dissolved in a mixture of water and organic solvent in a specified proportion into a round bottom flask. The mixture is reacted for short time of about one to two minutes at 60^0C in the microwave oven. After the reaction completes, adequate amount of solvent mixture is added to the above reaction

mixture to remove the residual, uncomplexed free drug and cyclodextrin. The precipitate so obtained is separated using whatman filter paper, and dried in vacuum oven at 40^0C for 48 hrs. [34]

Supercritical anti-solvent method

The cyclodextrin and drug is dissolved in a solvent. The solution is then fed into a pressure vessel under supercritical conditions, through a nozzle (i.e. sprayed into supercritical fluid anti-solvent). When the solution is sprayed into supercritical fluid anti-solvent, the anti-solvent rapidly diffuses into that liquid solvent as the carrier liquid solvent counter diffuses into the anti-solvent. The mixture becomes supersaturated and resulting precipitation of solute occurs. The remaining solvent is carried away with the supercritical fluid flow. [35]

Cyclodextrins Effects on Important Drug Properties in Formulation

The uses and benefits of cyclodextrins complexation are well recognized in pharmaceutical industries that were evidenced by several reviews in the past years. These benefits are bioavailability enhancement, active stabilization, odor or taste masking, irritation reduction and material handling benefits. Practical use of natural cyclodextrins as drug carries is restricted owing to their low aqueous solubility. The β-cyclodextrins is essentially nontoxic when given orally but it cannot be given in parenteral preparation owing to its low aqueous solubility and nephrotoxicity. Rate of metabolism of α-cyclodextrin is slower and that of γ-cyclodextrin is much faster than that of β-cyclodextrin. Cyclodextrins are metabolized in the colon. Cyclodextrins are used to improve the stability of substances to increase their resistance to hydrolysis, oxidation, heat, light and metal salts. Cyclodextrins can be applied to reduce the effects of bitter or irritant tasting and bad smelling drugs. Cyclodextrins are used for protection against degradation of substances by microorganisms. Cyclodextrins are useful for masking pigments or the color of substances. [36, 37 and 38]

Effect of cyclodextrins on drug bioavailability

The cyclodextrins enhances the bioavailability of insoluble drugs by increasing its drug solubility, dissolution and drug permeability. This is achieved by masking the drug available at the surface of the biological barrier, e.g. skin, mucosa or the eye cornea, from where it partitions into the membrane without disrupting the lipid layers of the barrier. In case of water soluble drugs, cyclodextrins increase the drug permeability by direct action on mucosal membranes and enhance drug absorption and bioavailability. It was reported that cyclodextrins, because of their ability to remove cholesterol, may increase membrane fluidity and induced membrane invagination through a loss of bending resistance and result in cell lyses. Labile drug stabilization by cyclodextrins and their ability to ameliorate drug irritation, and thus improve

drug contact time at the absorption site in nasal, ocular, rectal and transdermal delivery.[39]

Effect of cyclodextrins on drug stability

Cyclodextrins can improve the stability of several labile drugs against dehydration, hydrolysis, oxidation and photo decomposition and thus increase the shelf life of drugs. When a molecule is constrained within the cyclodextrin cavity, it is difficult for reactant to diffuse into cavity and react with the protected guest. It has been reported that cyclodextrin induced "enhancement of drug stability" may result of inhibition of drug interaction with vehicles and due to the inhibition of drug bioconversion at the absorption site. Large drug molecules like proteins and peptides can also form complexes with cyclodextrin and thus complexation result in both enhanced physical and chemical stability of this type of peptide drug. The stabilizing effect of cyclodextrins depends on the nature and induced functional group. The cyclodextrins were reported to have improved the photo stability of Trimeprazine and Promethazine. [40]

Effect of cyclodextrins on odor or taste masking of drug

Cyclodextrin complexation is a useful technique to suppress the bitter taste of drugs like Oxyphenonium bromide. With assumption that only the free drug molecule is responsible for bitter taste, the extent of the bitterness was reported to be dependent on the availability of free drug molecule, regardless the nature and the concentration of cyclodextrin.[40]

Effect of cyclodextrins on drug safety

The increased drug efficacy and potency, caused by cyclodextrin increased drug solubility, may reduce drug toxicity by masking the drug effective at lower doses. The toxicities associated with crystallization of poorly water soluble drugs in parenteral formulations can often be reduced by formation of soluble drug of cyclodextrin complexes. [41]

Effect of cyclodextrins on compatibility improvement

These are used for multiple ingredients or drug within a single formulation due the potential for synergistic benefits. Encapsulating one of the incompatible ingredients within a cyclodextrin molecule stabilizes in order to prevent chemical interaction.[42]

Effect of cyclodextrins on material handling improvement

Active ingredients like oils or liquids or volatile materials are difficult to handle and also difficult to formulate into solid dosage forms. Encapsulating these types of substances, cyclodextrin convert them into solid powder that has good flow properties and can be conveniently formulated into a tablet by conventional production processes and equipments.[43]

APPLICATIONS OF CYCLODEXTRINS

Characteristics of cyclodextrins are used in almost every drug delivery system. There are large

numbers of references and marketed products are available for application in drug delivery system. For e.g. cyclodextrin in oral drug delivery, sublingual, ocular, nasal, rectal, pulmonary, dermal and other novel drug delivery systems.

Oral drug delivery system

Applications of cyclodextrins in oral drug delivery include increased drug bioavailability due to increased drug solubility, improvement of rate and extent of dissolution and stability of the drug at the absorption site. Dissolution rate of poorly water soluble drug is responsible for both the rate and extent of oral bioavailability of the drug. The hydrophilic cyclodextrins are applied to enhance the oral bioavailability of steroids, cardiac glycosides, non-steroidal anti-inflammatory drugs, barbiturates, antiepileptic, benzodiazepines, antidiabetics, vasodilators etc. The immediate release formulations of analgesics, antipyretics, coronary vasodilators etc. are very useful in emergency situations.[44]

Rectal drug delivery system

Rectal delivery system is useful for those drugs having bitter or nauseous taste, have first pass metabolism and degrade in the stomach pH. It is an ideal route of administration for unconscious patients, children and infants. Hydrophilic cyclodextrins enhance the release of poorly water soluble from the oleaginous suppository base because of the lesser interaction of the resultant complexes with the vehicle. The complexation of lipophilic drugs with the hydrophilic cyclodextrins makes them insoluble in hydrophobic vehicles. One of the most important functions in designing a rectal drug delivery system is the release of drug from base. Since the rectal fluid is small in volume, viscous nature as compared to GI fluid. Cyclodextrins enhance the rectal absorption of in absorbable, hydrophilic drugs such as antibiotics, peptides, and proteins by their direct action on the rectal epithelial cells. The methylated cyclodextrins significantly enhance the rectal absorption of hydrophobic drugs, which are anti-inflammatory agents, like Flurbiprofen, Carmofur and Biphenyl acetic acids from the oleaginous suppository.[45]

Transdermal drug delivery system

The main barrier for dermal drug absorption through the skin is outermost layer stratum corneum. To decrease its barrier properties used penetration enhancers like alcohol, fatty acids etc. Cyclodextrins improves the solubility and stability of drugs in the topical preparations, enhances the transdermal absorption of drugs, sustains the drug release from the vehicle and avoids undesirable side effects associated with dermally applied drugs. Cyclodextrins have significant safety margin in dermal application and can be used to optimize the transdermal delivery of drugs intended for local or systemic effect. In transdermal drug delivery systems,

hydrophilic, hydrophobic as well as ionizable cyclodextrins also used as carries for drugs.[45]

Nasal drug delivery system

The nasal route is another effective way to pass the hepatic first pass metabolism, due to good permeability properties of nasal mucosa. Cyclodextrins are used in nasal formulations to increase the aqueous solubility of lipophilic drugs. The lipophilic cyclodextrins acts as penetration enhancers, especially in nasal delivery of peptides. Nasal preparations must be critically evaluated for their possible effect on the nasal mucociliary functions, which defend the respiratory tract against noxious inhaled materials such as dust, allergens and bacteria. Cyclodextrins have very low local toxicity after nasal administration.[46]

Ocular drug delivery system

The outermost layer of the eye cornea is a lipophilic epithelium. Thus drug must be somewhat lipophilic to able to permeate through the cornea into the eye. Cyclodextrins will increase solubilization of drug and increase the amount of dissolved drug at the lipophilic membrane surface, but excess cyclodextrins will decrease the ability of the drug molecule. Cyclodextrins have also been used to reduce ocular drug irritation and to increase chemical stability of drug in aqueous solution. The administration of ophthalmic drugs in gel and in polymer matrix have been shown to increase the contact time of the drugs with the cornea, thereby the increasing the ocular bioavailability.[47]

Parenteral drug delivery system

α- Cyclodextrins and the derivatives of hydrophilic of β and γ-cyclodextrins can be used in parenteral formulations. The γ-cyclodextrin forms visible aggregates in aqueous solution but it is not well suitable for parenteral formulations. In parenteral drug delivery applications of cyclodextrins are solubilization or reduction of drug irritation at the site of administrations, and stabilization of drugs unstable in the aqueous environment. The uses of cyclodextrins in parenteral drug delivery mostly studies of utilized sulfo butyl ether or hydroxypropyl derivatives of β-Cyclodextrin for enhancing the solubility of poorly soluble drugs. It is enable them to be delivered by the intravascular or the intramuscular route or to decrease the local irritation of drugs at the site of injection for stabilizing the drugs in an aqueous environment.[48]

Sublingual or buccal drug delivery system

Sublingual or buccal drug delivery is one of the ways to pass hepatic first pass metabolism. Aqueous solubility, dissolution and drug absorption are rate limiting steps for lipophilic drugs. Cyclodextrins based complex not only improves the drug absorption, but also mask the bitter taste of drugs.[49]

Pulmonary drug delivery system

Pulmonary drug delivery is also attractive route for systemic drug delivery and intended for local treatment of diseases like asthma, chronic obstructive pulmonary disease. Cyclodextrins increases the solubility, stability and dissolution rate of water insoluble and chemically unstable drugs.[50]

Controlled release drug delivery system

The most important property of cyclodextrins is to enhance the release rate of drugs from dosage forms and also to evaluate cyclodextrins as carriers in controlled release drug delivery systems. Complexation of drugs with cyclodextrins has been used to prepare polymeric drug systems such as microspheres and nanospheres to increase the solubility of the drugs or the loading capacity of drug delivery systems. The ionizable cyclodextrins derivative improves inclusion capacity, modify drug dissolution rate, and alleviate drug irritation. Compositions with cyclodextrins have been used for controlled release of drugs from matrix tablets such as Prednisolone.[51]

Novel drug delivery system

Cyclodextrins have applications in the design of drug delivery systems like liposomes, microspheres, nanoparticles, osmotic delivery, peptides and protein delivery.[52]

Cyclodextrins in chemical industry

Cyclodextrins and their derivatives in the chemical industry are used as catalysts to improve the selectivity of reaction, as reaction inhibitors, as well as for the purification and separation of industrial scale products. In the chemical industry, cyclodextrins are widely used to separate isomers and enantiomers. Cyclodextrins are widely used in the separation of enantiomers by high performances liquid chromatography (HPLC) or gas chromatography. Cyclodextrins can play a major role in environmental science in terms of solubilization of organic contaminants, enrichments and removal of organic pollutants and heavy metals from soil, water and atmosphere. Cyclodextrins are also applied in water treatments to increase the stabilizing action, encapsulation and adsorption of contaminants.[53]

Cyclodextrins in cosmetics, personal care and toiletries

In many personal care products triclosan acts as a topical antiseptic and disinfectant and it is nearly insoluble in water, moderately soluble in alkaline solutions, and quite soluble in organic solvents. The cyclodextrin complex of tricolsan is soluble in water and gives clear solution. In cosmetic preparations, cyclodextrins are mainly used to increase water solubility of lipophilic guests, to convert the liquid or oily guests to powder form, to increase the physical and chemical stability of guest molecule by protecting against decomposition, oxidation, hydrolysis or loss by

evaporation, to minimize or prevent skin irritation, to prevent interaction between various formulation ingredients. Most perfume concentrate (rose oil, citral and citronellal), aromatic essential oils can be stabilized by complex formulation with cyclodextrin and can be used solid preparations, such as powdered detergents, perfumed tablets that dissolved easily in bath water. Fragrance compounds can be stabilized by cyclodextrin and coated with oils and incorporated into soaps.[54]

Cyclodextrins in food and flavor

Cyclodextrins are used in food formulation for flavor protection or flavor delivery. They form inclusion complexes with a variety of molecules including fats, flavors and colors. Cyclodextrins have been used in food process with a variety of objectives. The most prevalent use of cyclodextrin in process aids is the removal of cholesterol from animal products such as eggs, dairy products. Fruits and vegetable juice are also treated with cyclodextrin to remove phenolic compound, which cause enzymatic browning. Flavonoids and terpenoids are good for human health because of their antioxidative and antimicrobial properties but they cannot be utilized as food stuffs owing to their very low aqueous solubility and bitter taste.[55]

Cyclodextrins in biotechnological field

The applications of cyclodextrin in biotechnological field began only in the 1980s and the majority of biotechnology processes mean an enzyme catalyzed transformation of a substrate in an aqueous medium. Cyclodextrins and its derivatives enhance the solubility of complexes in aqueous media and reduce their toxicity without damaging the microbial cells or the lipophilic substrates.[56]

CONCLUSION

Cyclodextrins are useful functional excipients, as result of their complexation ability and other versatile characteristics, are contributing to have different applications in different areas of drug delivery and pharmaceutical industry. Studies in both humans and animal have shown that cyclodextrins can be used to improve the drug delivery from almost any type of drug formulations. Cyclodextrins are not only well-known solubilizers, but constitute very powerful tool as permeation enhancers. Encapsulation of a guest molecule affects many of physicochemical properties of the guest molecule without affecting its intrinsic pharmacological activities. The ability of cyclodextrins to form complexes with a wide variety of organic compounds help to alter the apparent solubility of the molecule, to increase the stability of compound in the presence of light, heat and oxidizing conditions and to decrease volatility of compound.

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