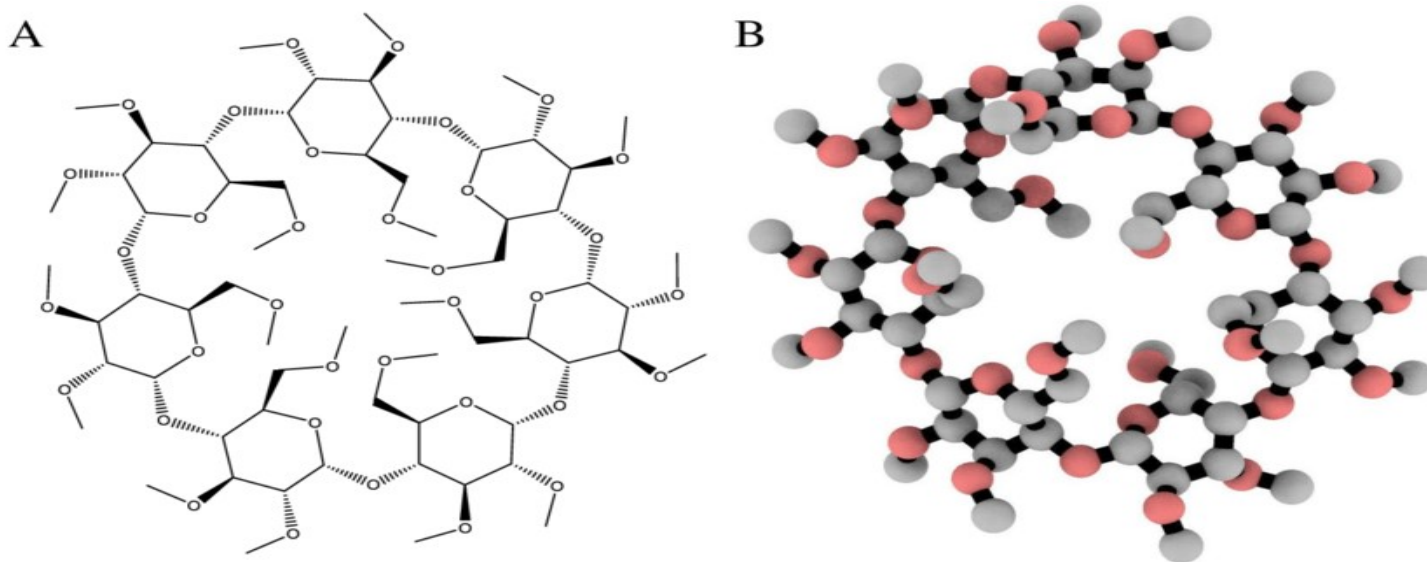


CYCLODEXTRINS



Supervised by: Assist.prof.Dr.Rita Sabah
Elias

Written by: Alaa Abdulamir

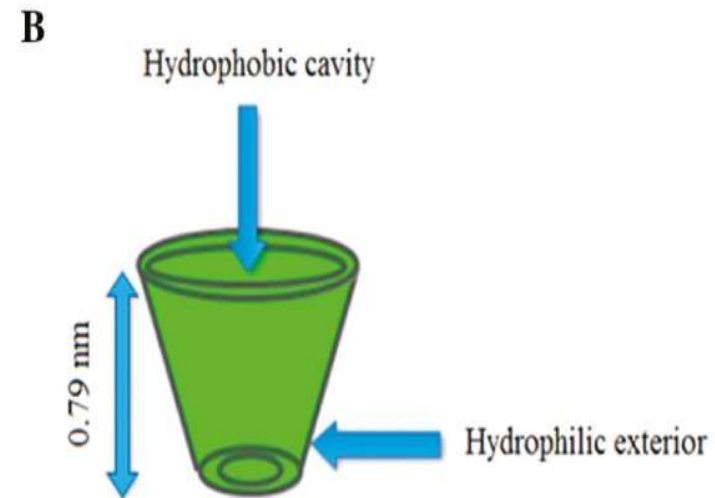
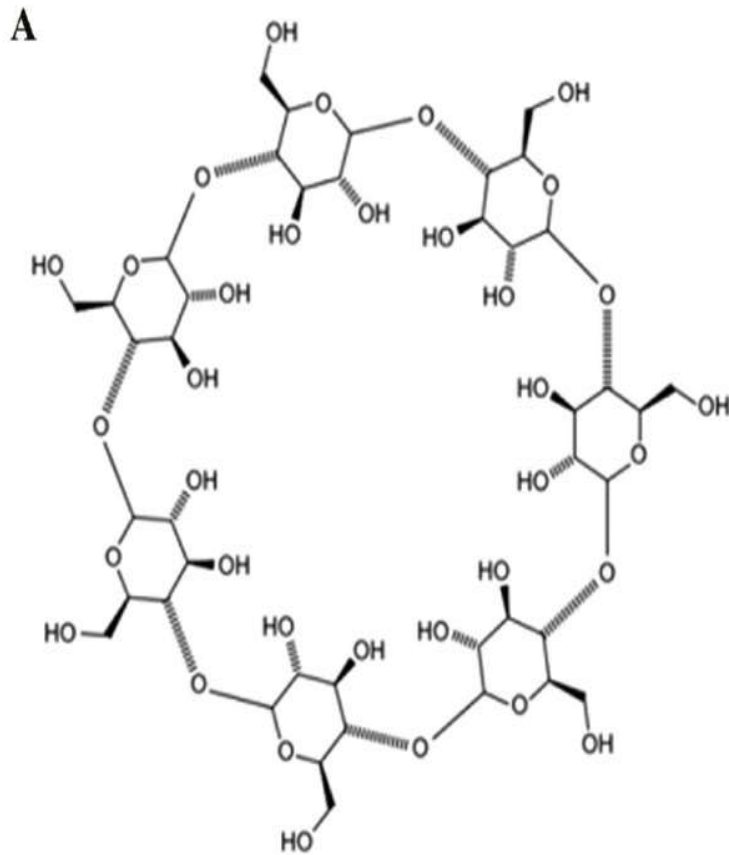
CONTENT

- ❖ INTRODUCTION
- ❖ STRUCTURES OF CYCLODEXTRIN
- ❖ TYPES AND PROPERTIES OF CYCLODEXTRIN
- ❖ CD'S DERIVATIVES
- ❖ PRODUCTION OF CYCLODEXTRIN
- ❖ INCLUSION COMPLEX
- ❖ COMPLEXATION TECHNIQUES
- ❖ TOXICOLOGICAL CONSIDERATION
- ❖ APPLICATIONS OF CYCLODEXTRIN
- ❖ CDs IN DRUG DELIVERY
- ❖ CONCLUSION
- ❖ REFERENCE

INTRODUCTION

- ❖ cyclic oligosaccharides arise from starch degradation via enzymes CGTases, with 6, 7 or 8 glucose residues and , that appear as α -, β - and γ -CDs and are linked by α -(1-4) glycosidic bond.
- ❖ CDs molecules have a truncated cone shape.
- ❖ Ics.
- ❖ In the pharmaceutical industry , CDs used as drug carriers.

STRUCTURES OF CYCLODEXTRIN



TYPES AND PROPERTIES OF CYCLODEXTRIN

α -CDs

- ❖ 6 membered sugar ring molecules
- ❖ relatively irritating after i.m. injection
- ❖ Binds lipids

β -CDs

- ❖ 7 membered sugar ring molecules
- ❖ Less irritating after i.m. injection
- ❖ Binds colestrols

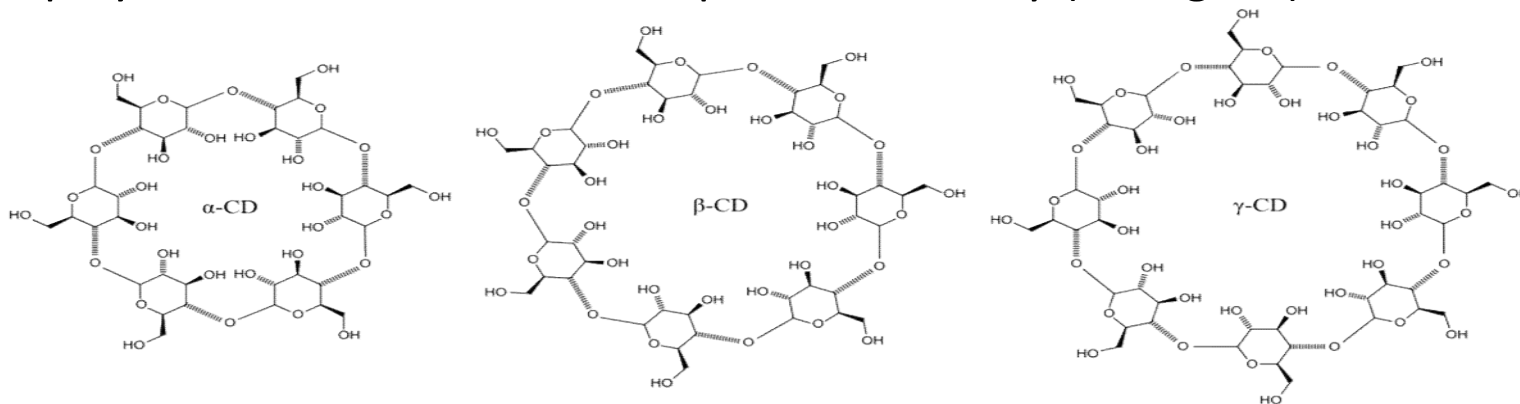
γ -CDs

- ❖ 8 membered sugar ring molecules
- ❖ insignificant irritation after i.m. injection

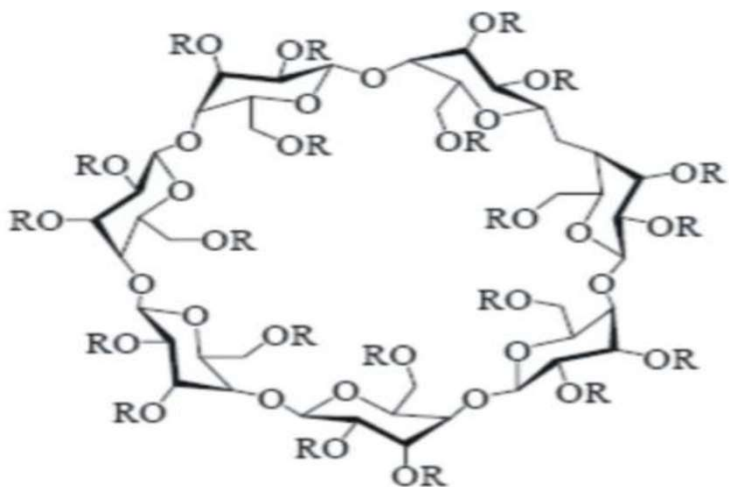
CONTINUE

Type of cyclodextrin	No. of Glucose units	Molecular weight	Molecular Dimensions (Å)			Solubility at 25oC (g/100ml H2O)
			Inside diameter	Outside diameter	Height	
α	6	973	5.7	13.7	7.0	14.50
β	7	1135	7.8	15.3	7.0	1.85
γ	8	1295	9.5	16.9	7.0	23.20

- ❖ The natural α - and β -cyclodextrins, unlike γ -cyclodextrin
- ❖ β -cyclodextrin, have limited aqueous solubility (1.85 g/ml) << derivatives



SOME DERIVATIVES OF β -CD AND ITS SOLUBILITY



Cyclodextrin	R = H or	Solubility in water (mg/ml)
β-Cyclodextrin	-H	18.5 mg/ml
2-Hydroxypropyl-β-cyclodextrin	-CH ₂ CHOHCH ₃	>600 mg/ml
Sulfobutylether β-cyclodextrin sodium salt	-(CH ₂) ₄ SO ₃ - Na ⁺	>500 mg/ml
Randomly methylated β cyclodextrin	-CH ₃	>500 mg/ml
Branched β-cyclodextrin	Glucose or maltose group	>500 mg/ml

CD'S DERIVATIVES

- ❖ Hydrophilic derivatives
- ❖ Hydrophobic derivatives
- ❖ Ionizable derivatives

PRODUCTION OF CYCLODEXTRIN

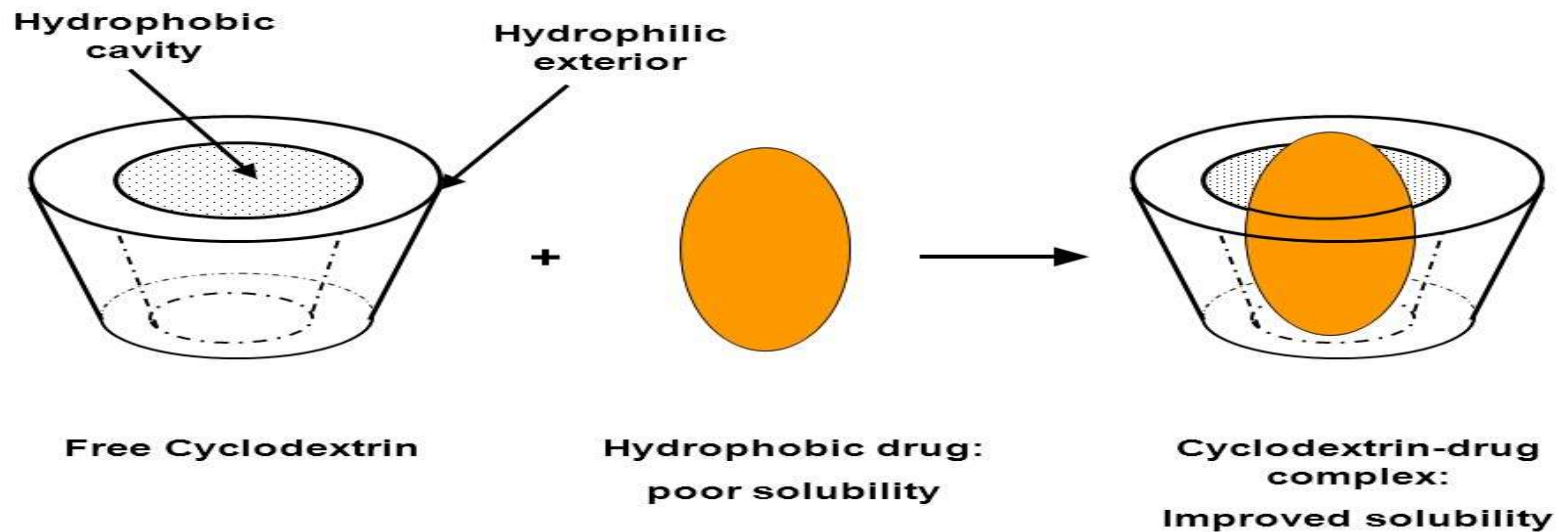
- ❖ Traditional method : by starch with amylase from *Bacillus macerans*
- ❖ Modern method: by Genetic engineering

FACTORS THAT CAN IMPROVE THE PRODUCTION OF CDS

- ❖ Solution
- ❖ Temperature effect
- ❖ Solvent
- ❖ Volatile guests

Inclusion complex

- ❖ IC means encapsulation of drug molecules or at least part of molecule.



COMPLEXATION TECHNIQUES

- ❖ Co precipitation
- ❖ Slurry complextion
- ❖ Paste complextion
- ❖ Dry mixing

TOXICOLOGICAL CONSIDERATION

- ❖ Nephrotoxicity
- ❖ Irritation
- ❖ diarrhea

APPLICATIONS OF CYCLODEXTRIN

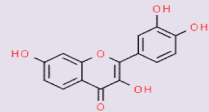
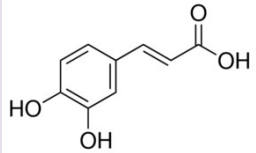
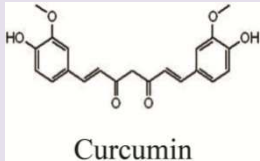
Due to their excellent ability to form molecular inclusion complexes. Cyclodextrins used in:

- ❖ Pharmaceutical chemistry
- ❖ Pharmaceutical industry
- ❖ Cosmetic and hygiene
- ❖ Food industry
- ❖ Paint industry
- ❖ Environmental protection

IN PHARMACEUTICAL CHEMISTRY

- ❖ CDs with flavonoids e.g. Reutin
- ❖ CDs with non flavonoids e.g. caffeic acid and curcumin.

CONTINUE

Class	Examples	Structure	CD	Improved characteristic
Flavonides (Flavone)	Rutin		β -CD HP- β -CD γ -CD HP- γ -CD	Solubility Stability Anti-oxidant Bioavailability
Non Flavonides (Phenolic acid)	Caffeic acid		β -CD HP- β -CD	Solubility
Non Flavonides (Alkaloids)	Curcumin	 Curcumin	α -CD HP- α -CD β -CD HP- β -CD RM- β -CD SBE- β -CD HTA- β -CD HP- γ -CD γ -CD	Solubility Anti-carcinogenic Transdermal permeation Anti-inflammatory Bioavailability Photodegradation

CDs IN DRUG DELIVERY

- ❖ Class II (poorly soluble/highly permeable)
- ❖ Class IV (poorly soluble/poorly permeable)

SOME EXAMPLES OF DRUGS CONTAIN CDs

Drug	Formulation	Trade name
α-Cyclodextrin Alprostadil (PGE1)	IV solution	Prostavasin
β-Cyclodextrin Dexamethasone Nicotine Nitroglycerin Piroxicam	Dermal ointment Sublingual tablet Sublingual tablet Oral tablet	Glymesason Nicorette Nitropen Brexin
2-Hydroxypropyl-β-cyclodextrin Indomethacin Itraconazole	Eye drop solution Oral and IV solutions	Indocid Sporanox
Randomly methylated β –cyclodextrin 17β-Oestradiol	Nasal spray	Aerodiol
Sulfobutylether β-cyclodextrin Voriconazole	IV solution	Vfend
2-Hydroxypropyl-γ-cyclodextrin Diclofenac sodium	Eye drop solution	Voltaren ophtha

conclusion

- ❖ Cyclodextrins are a family of macrocyclic oligosaccharides arising from the degradation of starch by the action of cyclodextrin glucosyltransferase that joined by α -1,4 glycoside bonds consisting of 6, 7 and 8 glucose units are called α -, β - and γ -cyclodextrin, respectively. with a hydrophilic outer surface and a lipophilic central cavity. In the pharmaceutical chemistry cyclodextrins have mainly been used as complexing agents to increase aqueous solubility of poorly soluble drugs, and to increase their bioavailability and stability. Studies in both humans and animals have shown that cyclodextrins can be used to improve drug delivery from almost any type of drug formulation.

REFERENCE

- ❖ 1) Pinho, E., Grootveld, M., Soares, G., & Henriques, M., Cyclodextrins as Encapsulation Agents for Plant Bioactive Compounds, *Carbohydrate Polymers* (2013)
- ❖ 2) T. Loftsson. A. Magnúsdóttir, M. Másson and T. Loftsson, *J. Incl. Phenom. Macroc.Chem* The conventional model of drug/cyclodextrin complex formation. *J. Pharm. Sci* (2002)
- ❖ 3) Sunil S. Jambhekar, S.S., Breen, P., Cyclodextrins in pharmaceutical formulations I: Structure and physicochemical properties, formation of complexes, and types of complex. (2015)
- ❖ 4)) T. Loftsson. A. Magnúsdóttir, M. Másson and T. Loftsson, *J. Incl. Phenom. Macroc.Chem* The conventional model of drug/cyclodextrin complex formation. *J. Pharm. Sci* (2002)

REFERENCE

- 5) Pinho, E., Grootveld, M., Soares, G., & Henriques, M.,
Cyclodextrins as Encapsulation Agents for Plant Bioactive Compounds,
Carbohydrate Polymers (2013)
- 6) Thorsteinn Loftsson a,* , Dominique Duch[^]ene b, Cyclodextrins and their
pharmaceutical applications, *International Journal of Pharmaceutics*, (2007)
- 7) E.M. Martin Del Valle, Cyclodextrins and their uses, *process
biochemistry*, (2013)
- 8- Sanjoy Kumar Das^{1,2*}, Rajan Rajabalaya³, Sheba David³, Nasimul Gani⁴,
Jasmina Khanam², Arunabha Nanda², Cyclodextrins-The Molecular
Container, *Research Journal of Pharmaceutical, Biological and Chemical
Sciences*, (2013)

REFERENCE

- ❖ 9) E.M. Martin Del Valle, Cyclodextrins and their uses, *process biochemistry*, (2013)
- ❖ 10) - Sanjoy Kumar Das^{1,2*}, Rajan Rajabalaya³, Sheba David³, Nasimul Gani⁴, Jasmina Khanam², Arunabha Nanda², Cyclodextrins-The Molecular Container, *Research Journal of Pharmaceutical, Biological and Chemical Sciences*, (2013)
- ❖ 11) T. Loftsson. A. Magnúsdóttir, M. Másson and T. Loftsson, *J. Incl. Phenom. Macrochem* The conventional model of drug/cyclodextrin complex formation. *J. Pharm. Sci* (2002)
- ❖ 12) Kurkov, S.V., Loftsson, T., *Cyclodextrins. Int J Pharmaceut* (2012)
- ❖ 13) E.M. Martin Del Valle, Cyclodextrins and their uses, *process biochemistry*, (2013)

REFERENCE

- ❖ 14) Pinho, E., Grootveld, M., Soares, G., & Henriques, M., Cyclodextrins as Encapsulation Agents for Plant Bioactive Compounds, *Carbohydrate Polymers* (2013)
- ❖ 15) Sanjoy Kumar Das^{1,2*}, Rajan Rajabalaya³, Sheba David³, Nasimul Gani⁴, Jasmina Khanam², Arunabha Nanda², Cyclodextrins-The Molecular Container, *Research Journal of Pharmaceutical, Biological and Chemical Sciences*, (2013)
- ❖ 16) LOFTSSON T: Cyclodextrins and the biopharmaceutics classification system. *J. Incl. Phenom. Macrocycl. Chem.* (2002).
- ❖ 17) Sanjoy Kumar Das^{1,2*}, Rajan Rajabalaya³, Sheba David³, Nasimul Gani⁴, Jasmina Khanam², Arunabha Nanda², Cyclodextrins-The Molecular Container, *Research Journal of Pharmaceutical, Biological and Chemical Sciences*, (2013)

..

