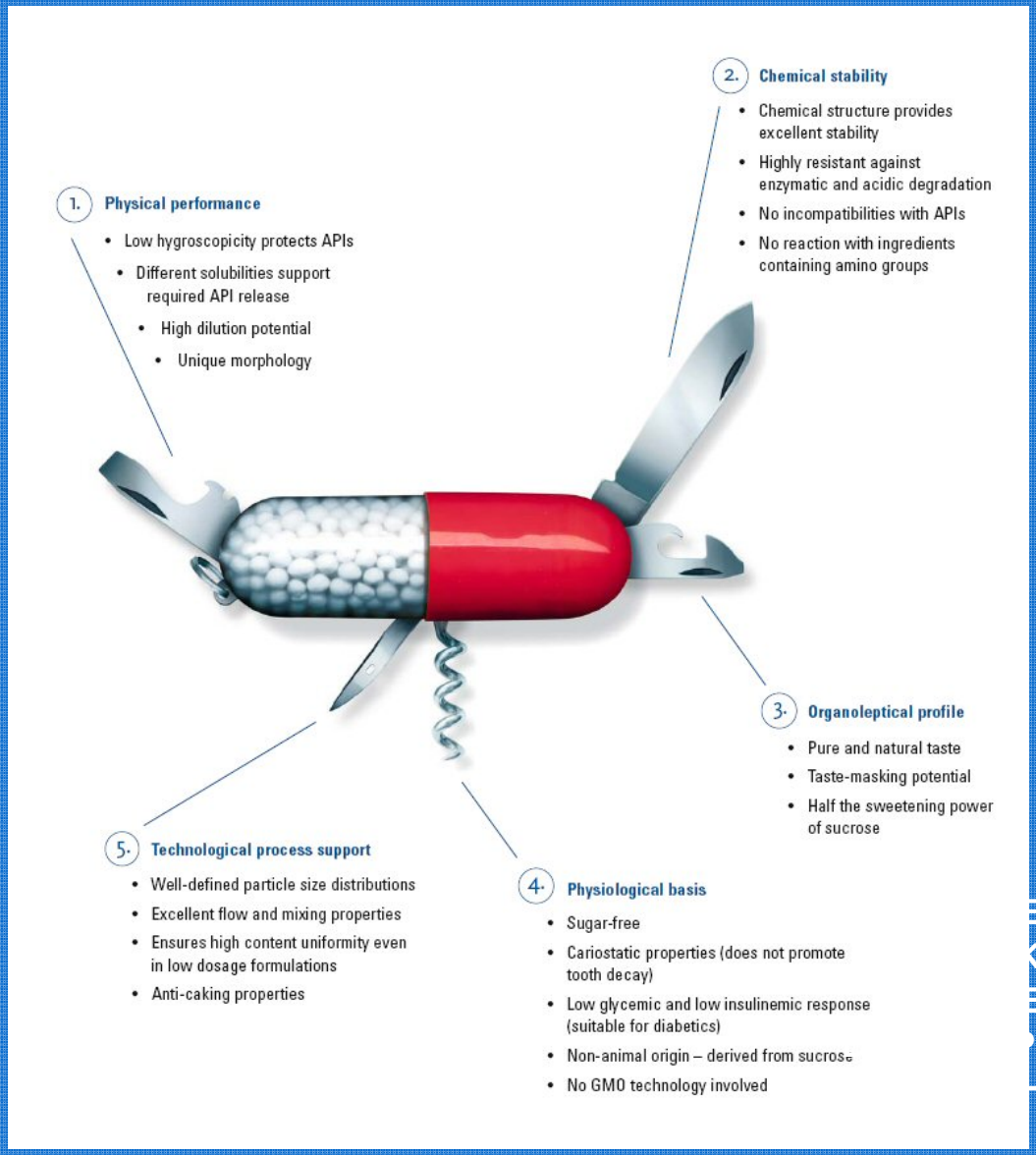
PHARMACEUTICAL AID

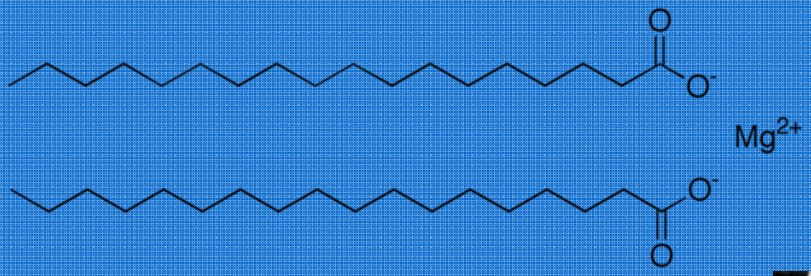


EPARED BY
KIRUTHIGA
ECTURER
HARMACEUTICAL
HEMISTRY

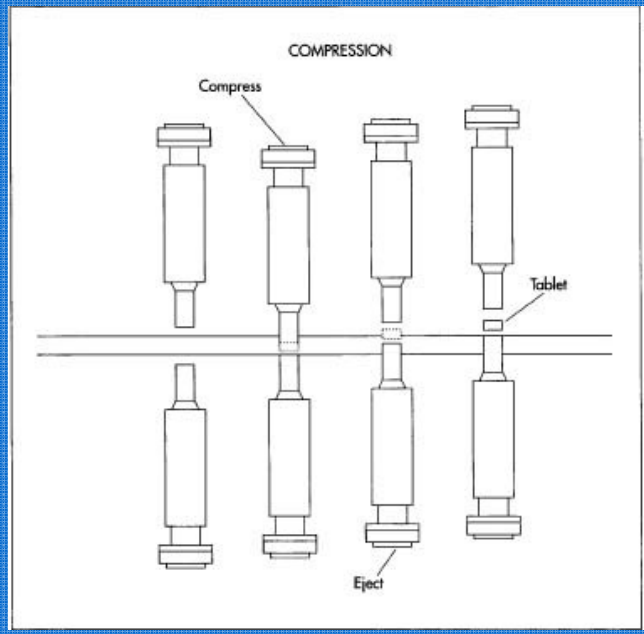
Excipients are inactive ingredients used as carriers for the active ingredients in a pharmaceutical product. These may be classified into the following categories:

- Antiadherents
- Binders
- Coatings
- Disintegrants
- Fillers and Diluents
- Coloring Agents
- Glidants
- Lubricants
- Preservatives
- Sorbents
- Sweeteners

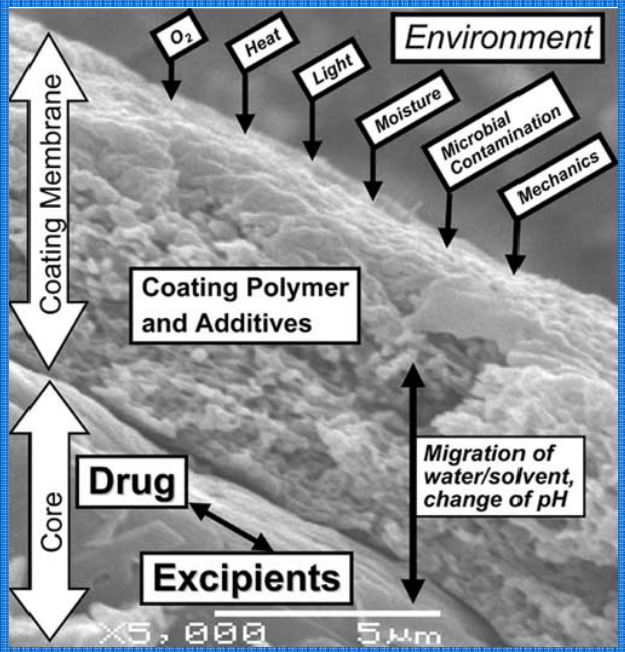
Antifrictional Agents and Antiadherents



Magnesium Stearate



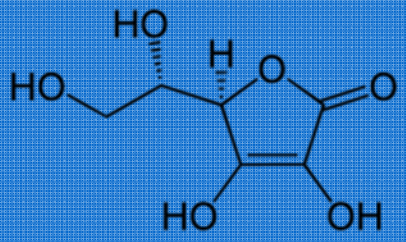
- Antiadherents are used to keep the powder from sticking to the tablet punch face during the manufacture of tablets.
- The most common is magnesium stearate



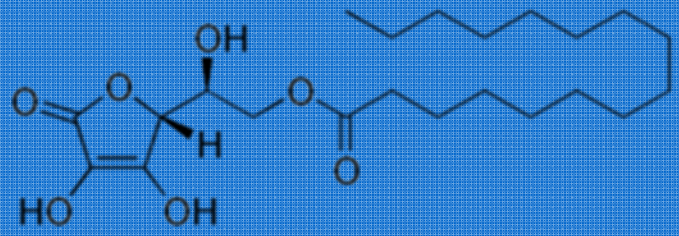
The pharmaceutical ingredients must be stabilized toward:

- Environmental factors (air, water vapor, sunlight)
- Interactions between different ingredients in the drug or different functionalities in the same molecule
- Manufacturing stress (sterilization, compaction, etc.)

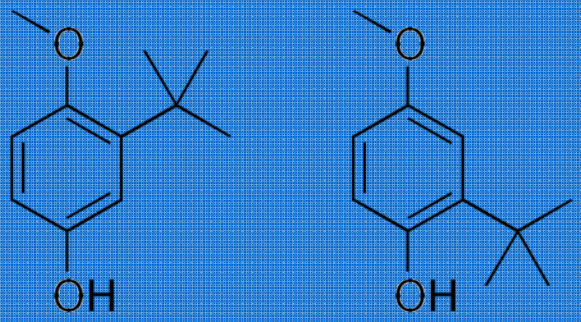
Antioxidants



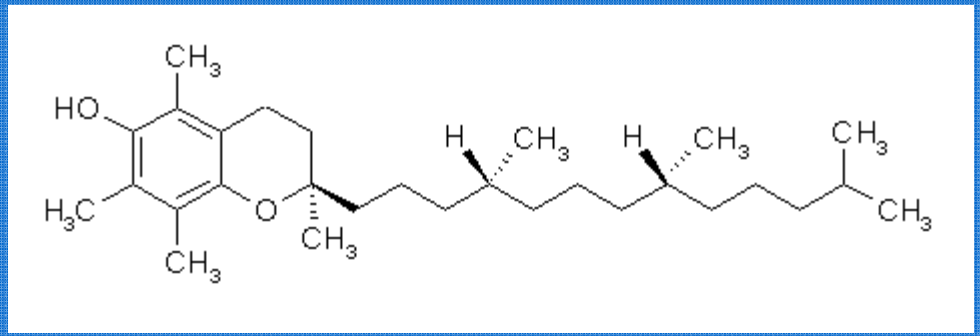
Ascorbic acid



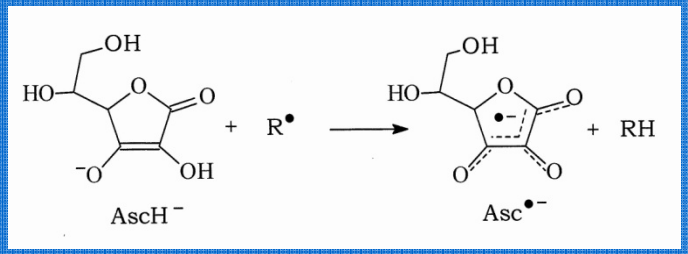
Ascorbyl Palmitate



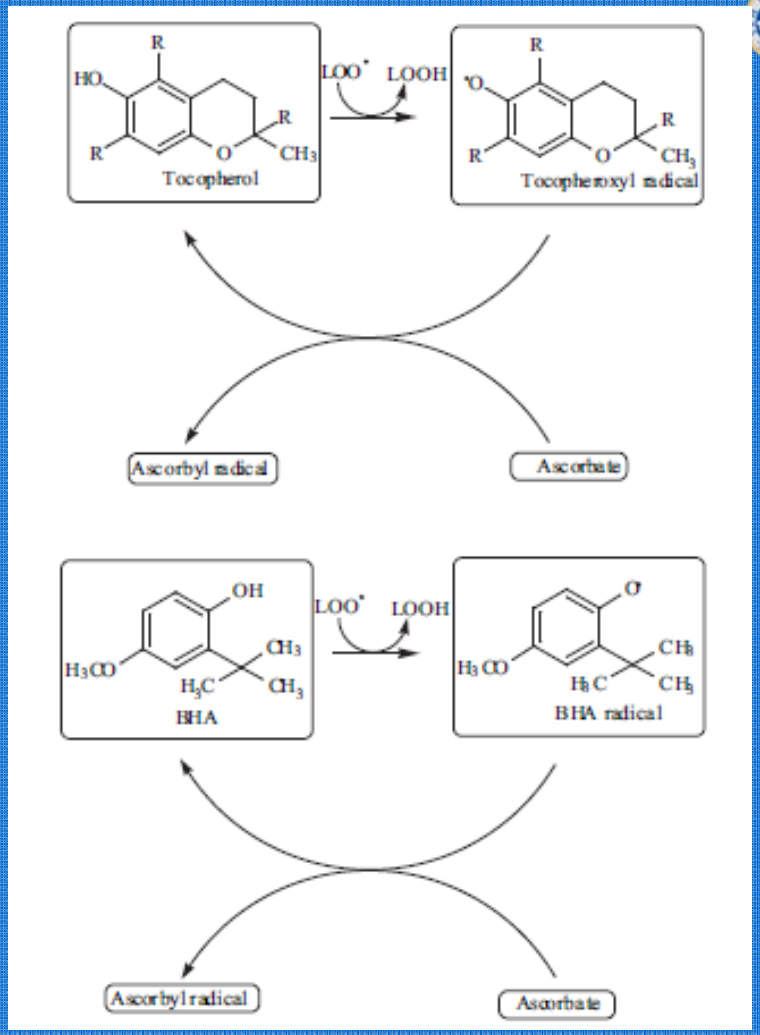
Butylated hydroxyanisole



Alpha-tocopherol

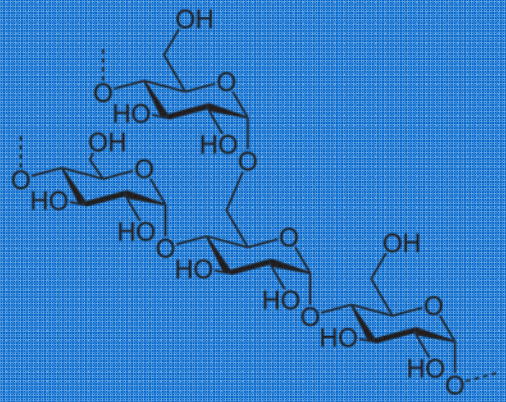


The Ascorbate Radical

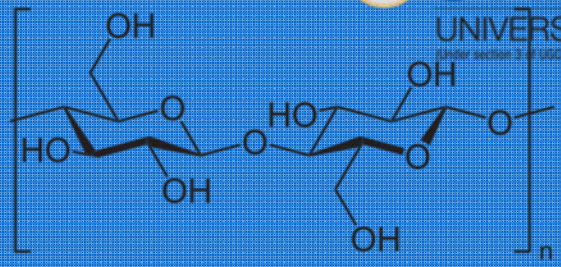


The phenolic antioxidants are frequently employed in smaller amounts, together with a larger amount of an ascorbic acid derivative, which serves to provide a hydrogen atom to the phenolic radical, thus regenerating the antioxidant species.

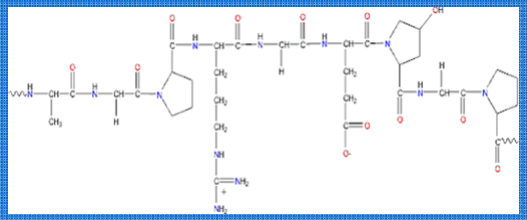
Binders



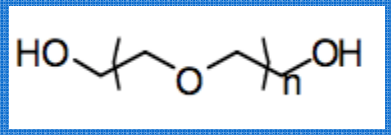
Starch
(1,4-alpha-glycosidic linkages)



Cellulose
(1,4-beta-glycosidic linkages)



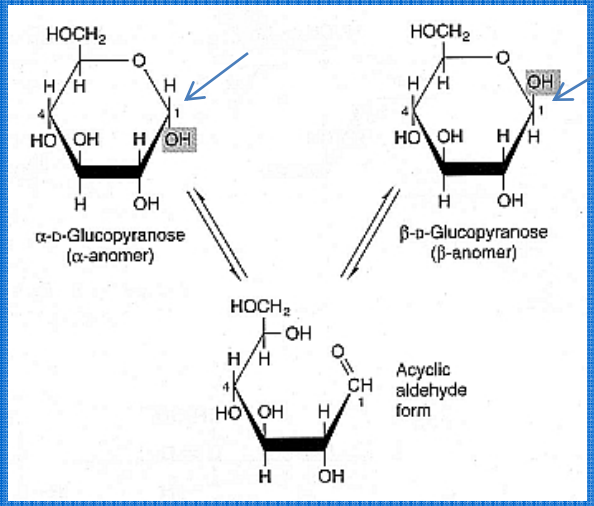
Gellatin



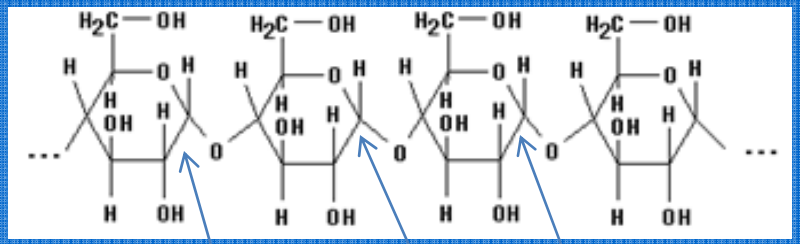
Polyethylene glycol (PEG)

Binders add mechanical strength to the tablet or granules.

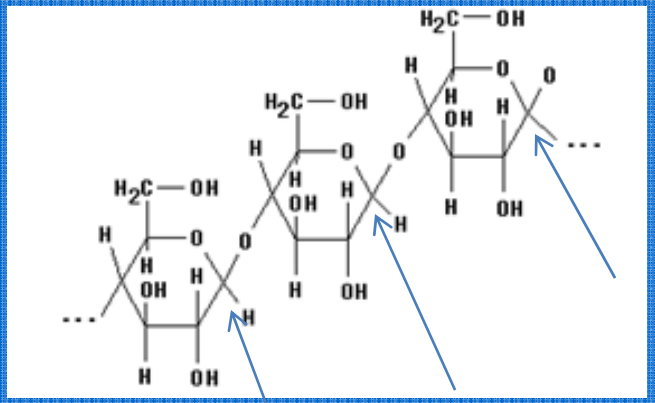
Monomeric glucose exists as a mixture of α and β-anomers



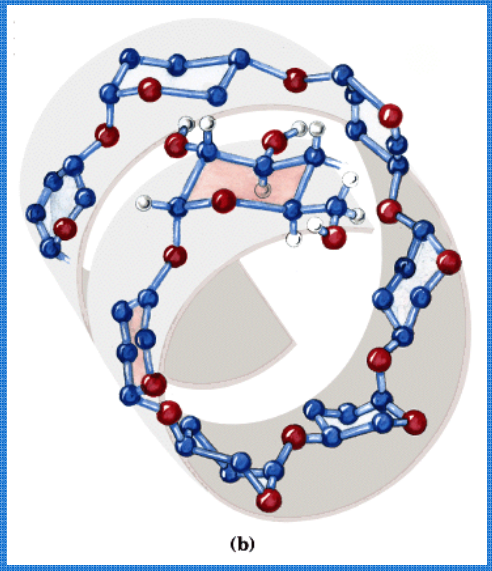
However, once the glucose is polymerized into starch or cellulose, the stereochemistry of the anomeric carbon is no longer in equilibrium.



Starch (100 to 6000 glucose units)
Starch has 1,4-alpha linkages



Cellulose (1800 to 3000 glucose units)
Cellulose has 1,4-beta linkages



Starch coil

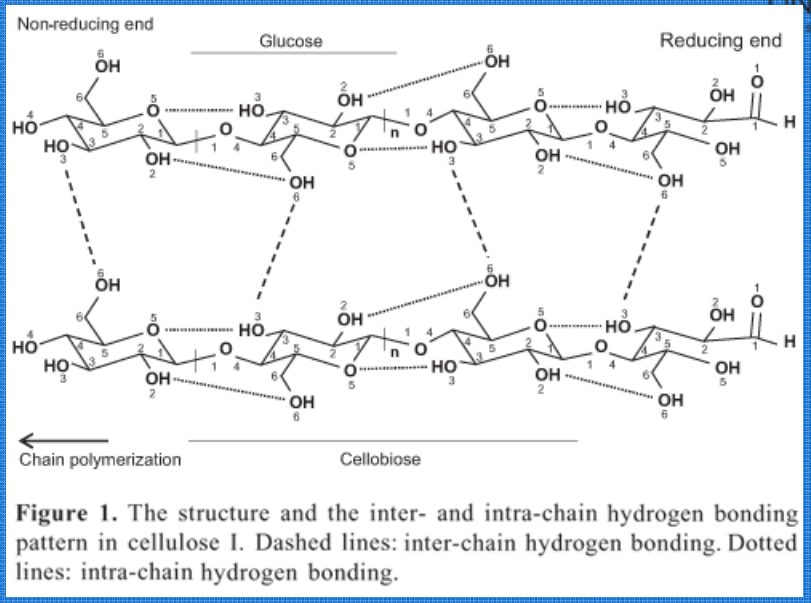
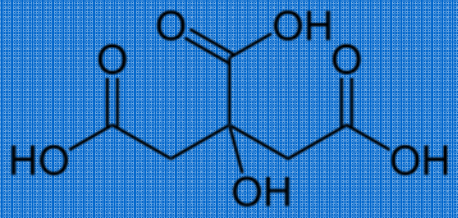


Figure 1. The structure and the inter- and intra-chain hydrogen bonding pattern in cellulose I. Dashed lines: inter-chain hydrogen bonding. Dotted lines: intra-chain hydrogen bonding.

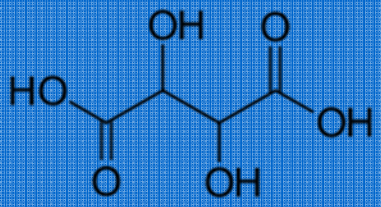
Linear Cellulose

Cellulose has an extended, and rather stiff conformation and is much less soluble and less digestible than is starch.

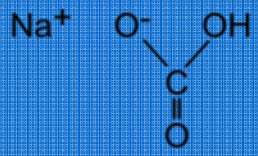
Buffering Agents



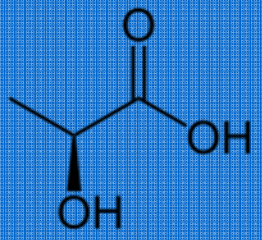
Citric Acid



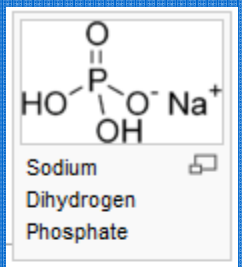
Tartaric Acid

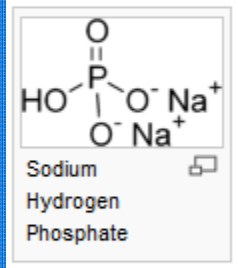


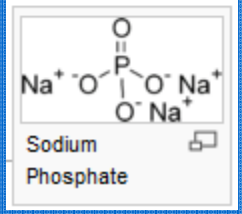
Sodium Bicarbonate



Lactic Acid

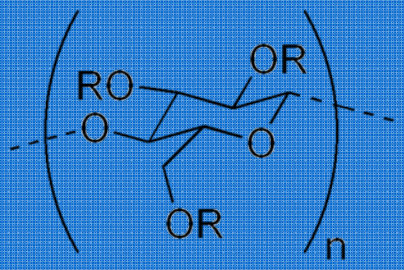






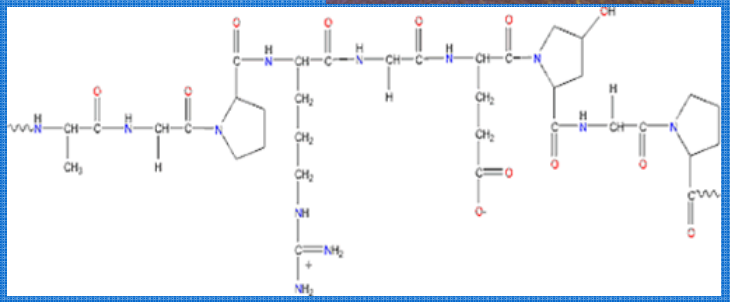
The pH of the preparation will need to be adjusted to maintain optimum effect and stability of the pharmaceutical.

Coatings



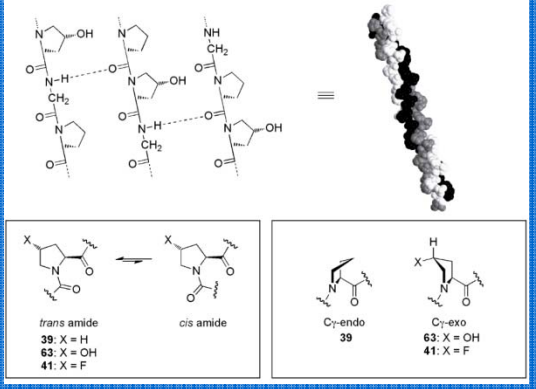
R = H or CH_3 or $CH_2CH(OH)CH_3$

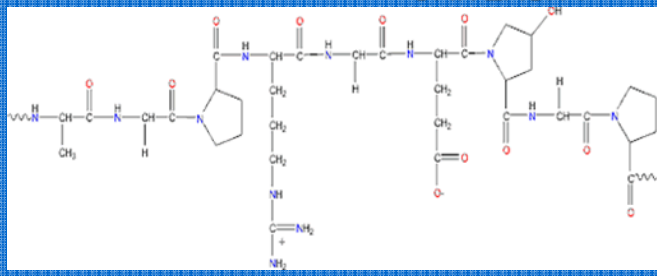
Hydroxypropylmethylcellulose



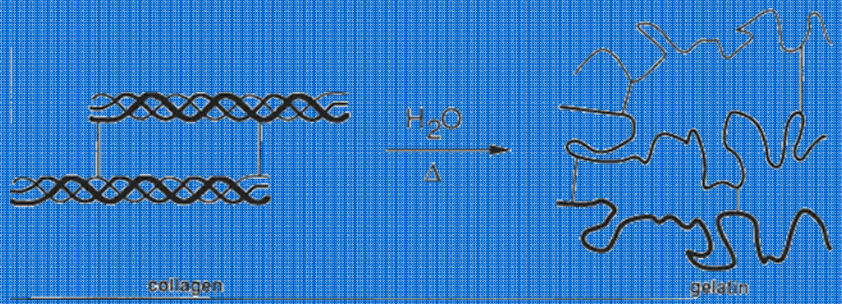
Gelatin

- Most coated tablets are coated with hydroxypropylcellulose
- Capsules are coated with gelatin

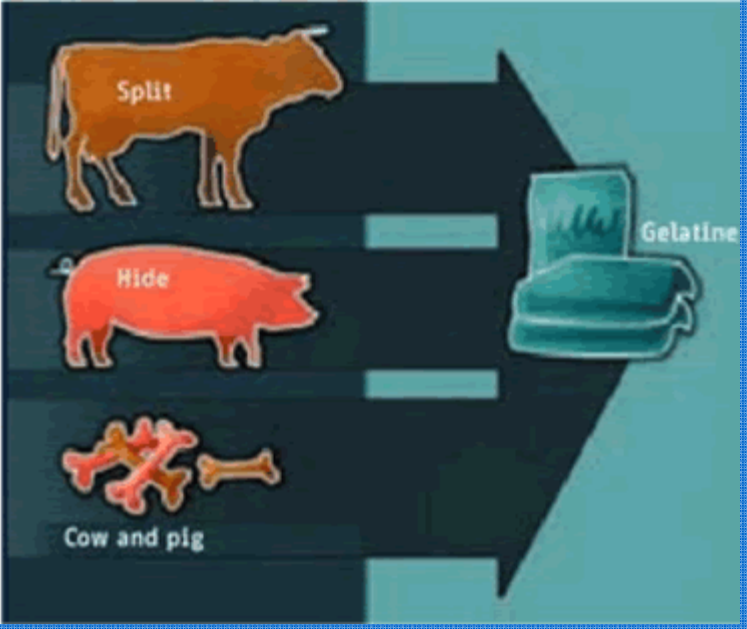


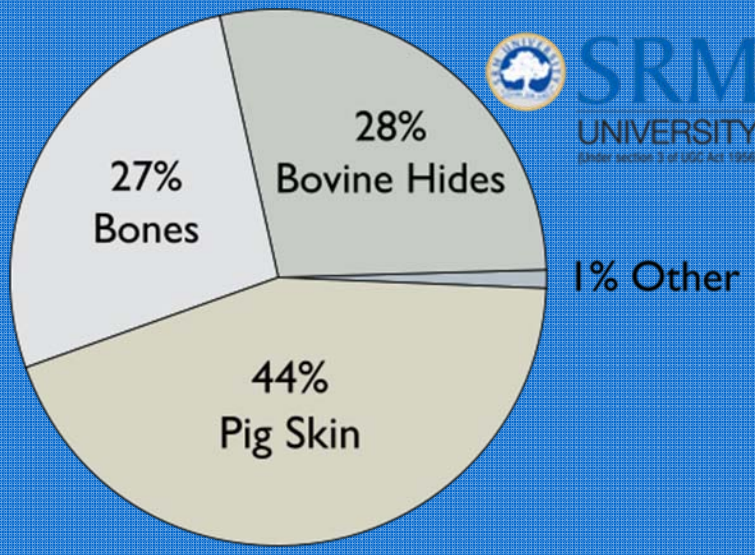


Collagen



Gelatin is made by denaturing the triple helix of collagen, a protein which provides structural stability to bones and muscle.

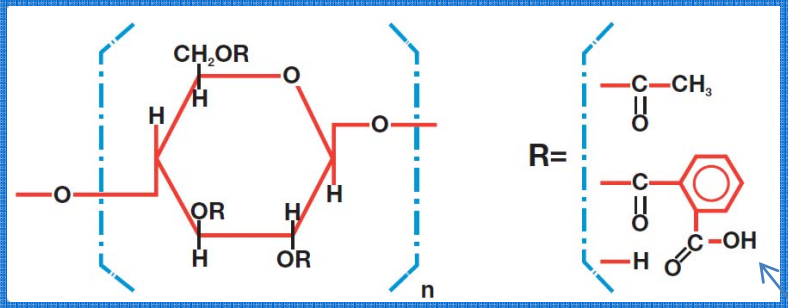




Materials Used in Gelatin Production

Gelatin is made by several processes which employ body parts from cattle, pigs, and horses and utilize chemical processes to achieve partial denaturation of the collagen.

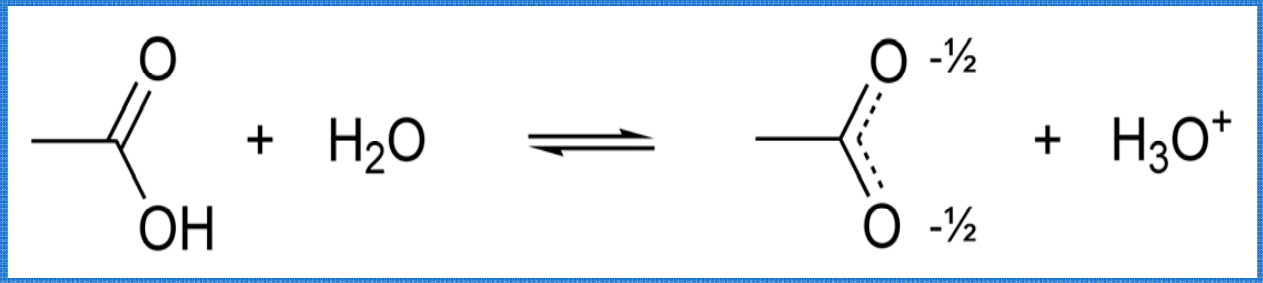
Enteric Coatings



Cellulose Acetate Phthalate (CAP)

Free carboxylic acid remains in polymer.
This is an acidic functionality and is deprotonated (ionized) at basic pH.

Tablets coated with enteric coatings will release their contents in the small intestine, not the stomach.
Such coatings are frequently used on products that my irritate the stomach, such as aspirin.
A commonly used coating material is cellulose acetate phthalate (CAP)



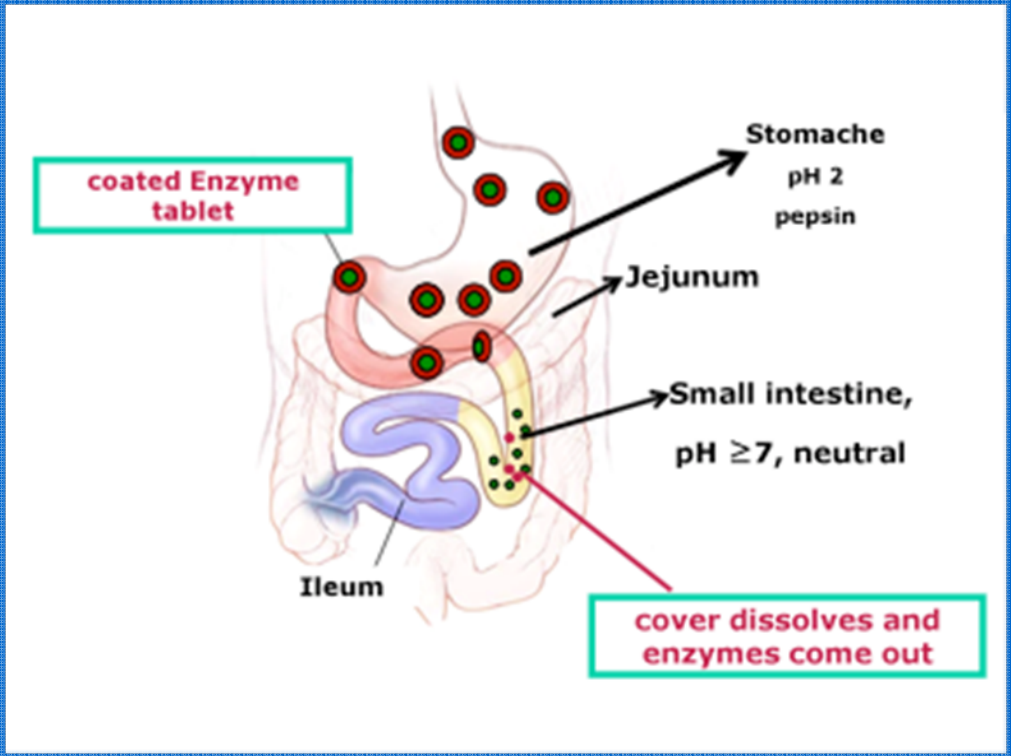
Non-water soluble

Water-soluble ionic form

$$K_a = \frac{[A^-][H^+]}{[HA]}$$

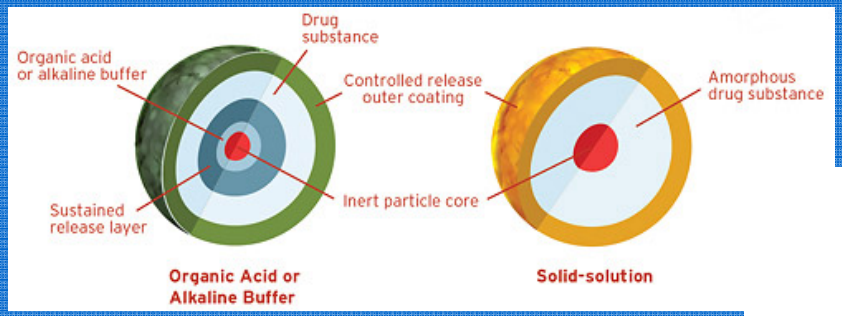
$$pH = pK_a - \log \frac{[A^-]}{[HA]}$$

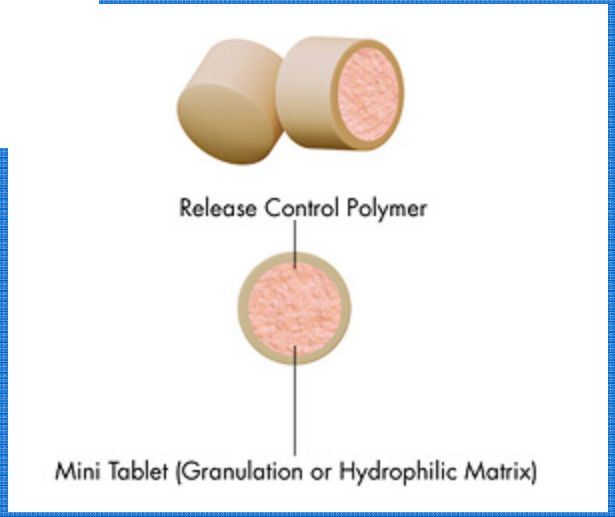
So, when [A-] = [HA], the pH = pKa.
The pKa of carboxylic acids is in the range of 3-5.
Thus carboxylic acids are protonated (nonionized) in the acidic environment of the stomach [pH = 2], but ionized in the more basic environment of the intestine [pH = 8].

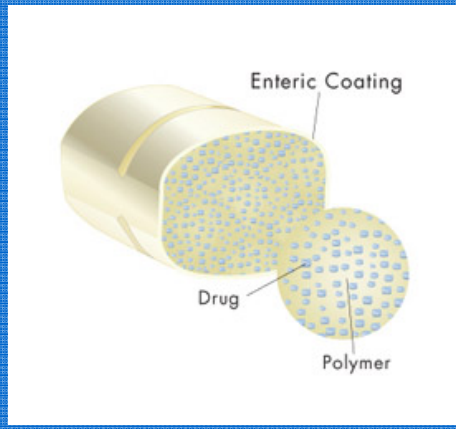


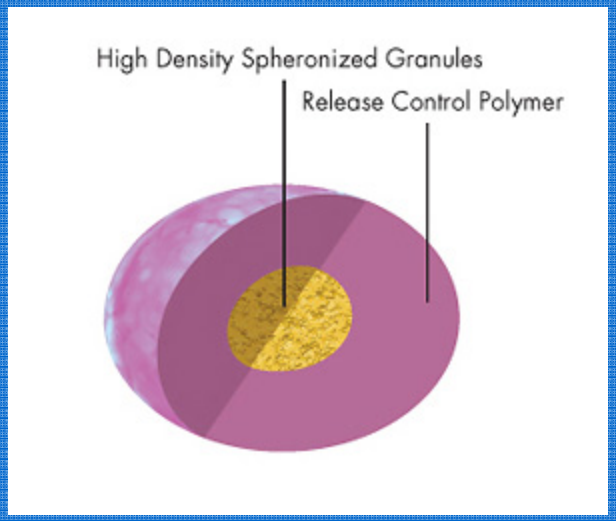
Thus the enteric coating becomes more water soluble (since it is in the ionic form, usually more water soluble than the nonionized form) in the intestine.

Sustained Release Technology



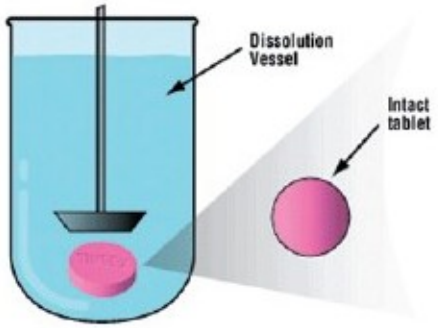




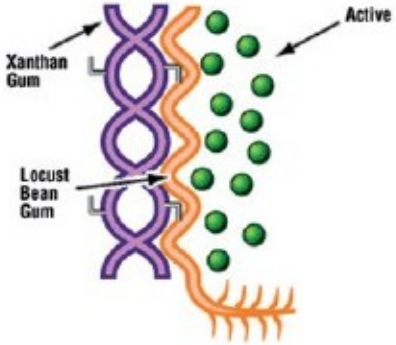


Most sustained release technology involves the slow transfer of the active ingredient through a polymer matrix.

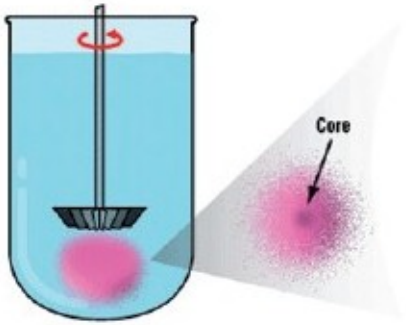
On initial exposure to water, the interface between water and the outer tablet begins. The inner tablet core remains unwetted because the outer portion of the tablet controls the rate of water ingress into the matrix.



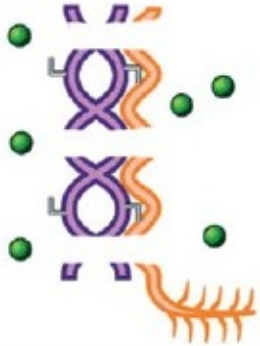
At time zero, the water starts hydrating the xanthan and locust bean gums.

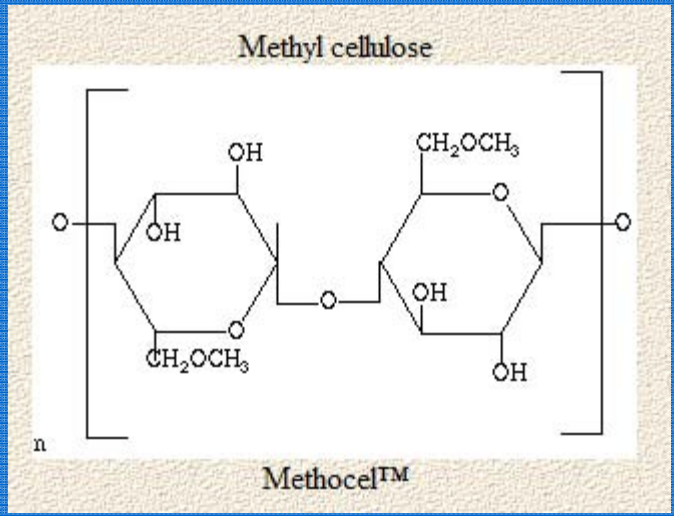


At 21 hours most of the matrix has eroded and a large percentage of the drug has been released.



The interface has continued to progress through the tablet allowing for more and more of the matrix to become wetted and gelled. The unwetted core reduces to only a very small percentage of the tablet.





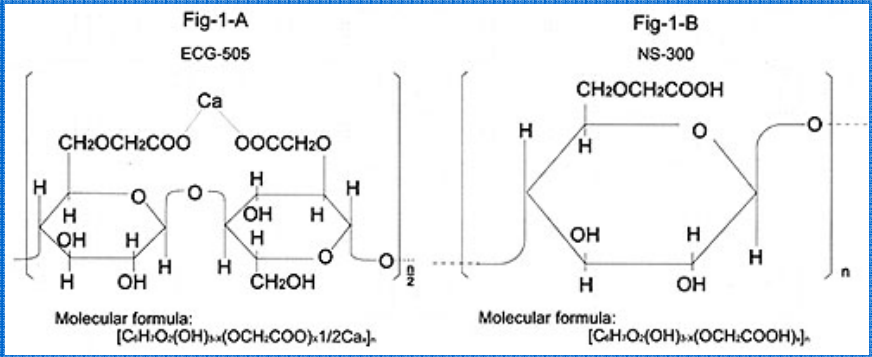
Dow Excipients

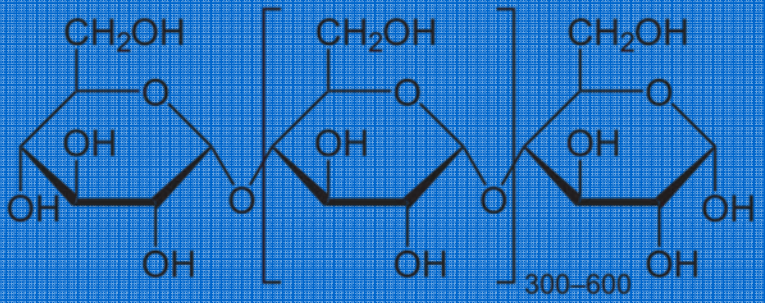
Controlled Release Systems

In a hydrophilic matrix system, a METHOCEL™ Premium CR cellulose ether or a POLYOX™ Water-Soluble Resin, NF Grade is uniformly incorporated throughout the tablet. Upon contact with water, it hydrates the outer tablet surface to form a gel layer. The rate of diffusion of drug out of the gel layer and the rate of tablet erosion control the overall dissolution rate and drug delivery.

METHOCEL™ Premium CR products and POLYOX™ Water-Soluble Resins, NF Grade are produced under controlled conditions that yield consistent properties and reproducible performance. They're not subject to the range of variability sometimes encountered with polymers like guar, shellac, and other botanic extracts.

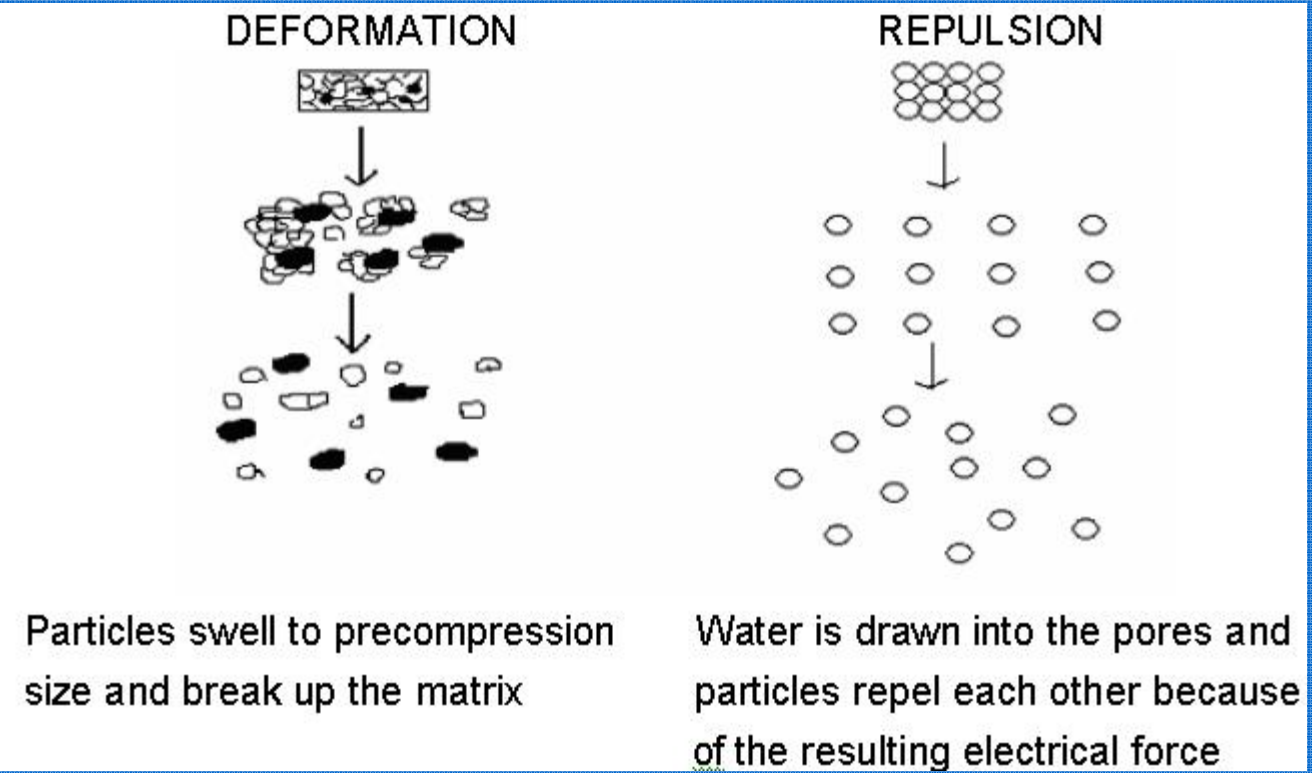
Disintegrants





Disintegrants are hydrophillic compounds that assist the break up of granules, tablets, and capsules

The most widely used are carboxymethyl cellulose calcium (left) and potato starch (right).



- During the compression process that is involved in generating a tablet, the starch particles are deformed.
- This deformation is relieved upon wetting and hydration of the starch, thus leading to breakup of the tablet.

THANK YOU