CAPSULE DOSAGE FORM

INTRODUCTION:

- Early 19th century, Mathes developed the first capsule dosage form from gelatin.
- Since then this technology has been continuously improved and refined, yielding range of capsule forms available today.
- Capsules are gelatin shells filled with the ingredients that make up an individual dose.
- Dry powders, semi-solids, and liquids that do not dissolve in gelatin may be encapsulated.
- Capsules account for about 20% of all prescriptions dispensed.

MAINLY TWO TYPES

1.HARD GELATIN CAPSULE

2.SOFT GELATIN CAPSULE

Capsules are used for filling different materials like
Powders, Granules, Beads, Tablets, Capsules, Pastes etc..

Some of the disadvantages associated with conventional capsule:

They are easily tampered with (although techniques exist for preventing this).
They are subject to the effects of relative humidity and to microbial contamination.

Some of the innovations are targeted to:

- Overcome the disadvantages associated with conventional capsules.
- Achieve modified drug release.
- Encapsulation of various kind of material.
- Modified applications

INNOVATIONS IN CAPSULES:

1) **Innovations in Capsule Shells**: it includes modification of capsule shell to improve shell property.
2) **Innovations in Capsule System**: it includes modification of the system to achieve modified release.

1]INNOVATIONS IN CAPSULE SHELLS:

Targeted to :

- Improvement in the shell property

- Provide physical strength
- Protection from moisture
- Protection from microbial contamination
- Protection from light and oxygen
- Improve compatibility of fill material with capsule shell.

IT INCLUDES:

Non animal Capsule

- HPMC Capsules
- Pullulan Capsules
- PVA Capsule
- Starch Capsule
- V Caps®

Animal Capsule

- Gelatine/ PEG Capsules
- Coni-Snap® Capsule(**OceanCaps)**
- Press-fit® Gelcaps
- LiCaps®
- Posilock
- Minicasule
- DBcaps® Capsules

HPMC CAPSULES(HYPROMELLOSE):

QUALI-V, developed by Shionogi Qualicaps, is the first HPMC capsule developed for eventual use in pharmaceutical products.

The features of QUALI-V are summarized as following:

- Made from **non-animal** materials,
- Chemically **stable.**
- **Low moisture content** than Gelatin capsule, as determined by Microbalance system.

- **Less brittle** even in low humidity(≤1% moisture content)
- Fast dissolution (No change in dissolution profile under stress conditions) and soluble in water at room temperature.
- No cross linking.
- **Lower water vapor permeability** than Gelatin capsule.**(Gelatin>PEG-Gelatin>HPMC)**
- Low static electricity and light protected.
- No Millard reaction with fillings.
- Not substrate for protease.
- High tolerance to temperature
- Chemical inactivity and solubility at room temperature.
- In these type of capsules powder, tablet, granules, pellets, liquids and semisolids are filled.
- Suited to automatic capsule filling machines.

QUALI-V®-I:

A New Key for Dry Powder Inhalers

- Superior physical performance a moisture contents
- Content could easily arise in the usage of DPIs with capsules.
- Better cutting and puncturing performance in standard DPIs.
- Elimination of the generation of shell particles in use.
- Excellent microbiological quality.
- Higher weight specification available if required.
- Suitable for use in all types of DPIs

PULLULAN CAPSULES:

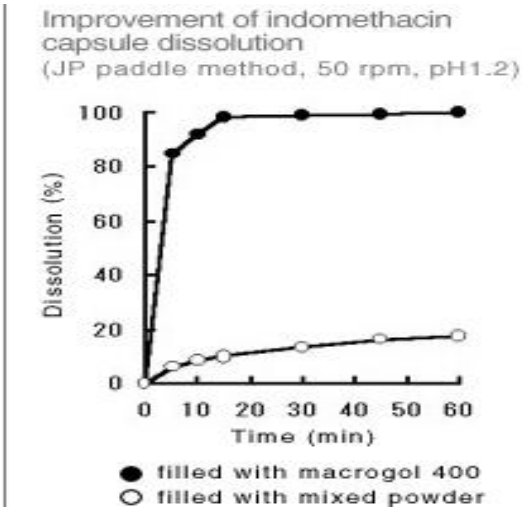
- Water-soluble polysaccharide
- Derived by bacterial fermentation from corn.
- Widely use in Japan
- They are odorless, tasteless, and completely biodegradable
- Used in production of foods, pharmaceuticals and cosmetics.
- The film formation properties of Pullulan are similar to gelatin.
- Dried capsules are comparatively weak in physical strength.
- Requires water to act as a film plasticizer, which may have a negative effect on active ingredients.
- Only one supplier of the raw material
- Does not show any meaningful advantages over hypromellose

NP Caps™:

- Made up of pullalan.
- Pullulan is very stable and well-characterized, and has achieved wide regulatory acceptance with its proven safety record.
- Its generally use for those people who are vegetarians, diabetics and patients with restricted diets.
- It is 100% natural they are Vegetable origin, No chemical modification, Non-GMO, Starch-free, Preservative-free, Gluten-free.

PVA CAPSULES:

- PONDAC Capsule (name)
- Insoluble drugs can be dissolved in solvents such as macrogol 400, being filled in capsules.
- The bioavailability of insoluble drugs can be improved very much.
- The oxygen permeability of PVA copolymer capsule is significantly low.
- The gelatin capsule was developed in the 19th century.
- The HPMC capsule was developed in the 20th century.
- The PONDAC capsule is the hope for the 21st century



STARCH CAPSULES:

- Made from potato starch and represent a direct alternative to hard gelatin capsule.
- Manufactured by the injection moulding technique developed by Capsugel (Capill®).
- Offers advantages like.
    - pH independent dissolution
    - Suitable for enteric coating
    - Tamper evident

- Produced from non-animal derived ingredients

- Consists cap and body; which are sealed together at the time of filling to prevent separation.
- Sealing is achieved by applying a hydro alcoholic solution to inner section of the cap, immediately prior to its being placed on to the body.
- Different size capsules are manufactured (number 0, 1, 2, 3, 4) by changing the mold.
- Officially recognized in USP 23 and NF 18

ENTERIC STARCH CAPSULES:

- Overcome coating problems encounter during coating of HGC.
- Coating of starch capsules appear to be less problematic because of the smooth seal, coupled with the higher bulk density of capsules, which provide for a more uniform coating bed.
- Stability of coated starch capsule evaluated.
- Eg. TARGIT®

VCaps®:

- Two-piece capsules made from cellulosic raw materials that satisfy vegetarian and cultural needs
- easy to swallow
- effectively mask taste and odor
- allow product visibility
- Vcaps capsules are also starch-free, gluten-free and preservative-free, and meet the strict dietary needs of customers that choose a vegetarian lifestyle.
- They are also Kosher and Halal certified.
- Vcaps vegetable capsules are manufactured in a GMP facility that meets ISO 9000 certification criteria.

GELATIN/PEG CAPSULES:

- Reduce the brittleness of standard gelatin capsules when exposed to a low-moisture content thus making the capsules more compatible to hygroscopic formulations or moisture-sensitive ingredients

Gelatin/PEG Features

- Less brittle
- Good for hygroscopic and moisture-sensitive ingredients
- Odorless, tasteless,three-year shelf life
- Available in sizes from 00 to 4
- The addition of PEG improves the mechanical strength of the capsule.

- At moisture contents between 8% - 12%, gelatin/PEG capsules have equivalent mechanical strength to standard gelatin capsules with moisture between 13% - 16%.

Gelatin/PEG capsules are available in commercial pharmaceutical products

- Cardiovascular (Tocopherol nicotinate)
- Vasodilators (Nifedipine)
- Antihypertensive (Captopril)
- Digestive Enzyme

Ocean CapsTM:

- ✓ OceanCapsTM is fish gelatin capsules
- ✓ It contain all-natural marine supplements
- ✓ Its over 40% of supplement users in France, Germany and the UK
- ✓ US consumers continue to move toward natural alternatives, and

look for products like marine supplements in fish capsules

- ✓ Ideally suited for fish-eating vegetarians looking for fish capsules,

and marine supplements such as fish oil, DHA, EPA, salmon liver oil, shark cartilage and glucosamine.

- ✓ Perfect for the supplement needs of fish-eating vegetarians, such as iron,zinc, calcium and vitamins B2 and B12
- ✓ Certified origin from high quality, farmed fish
- ✓ Preservative-free, starch-free, gluten-free

PRESS FIT® GELCAPS:

- a unique dosage form consisting of a high-gloss gelatin coating that encases a caplet core.
- Press-Fit gelcaps combine the best qualities of a gelatin capsule with the density of a tablet, creating an exciting new dosage form that can be custom engineered to meet specific product performance criteria.
- The elegant, geometric shape of Press-Fit gelcaps is distinct in the marketplace.
- The high gloss finish and extensive selection of color combinations provide additional opportunities for unique trade dress and enhanced consumer recognition.
- The outside gelatin shell is taste-free,
- Safe and effective utilization in oral dosage applications.

  Manufactured by exclusive cold- shrink process on a special filling and coating machine.

LICAPS®:

- Two-piece gelatin capsules that have been specially designed to be sealed for secure containment of liquids and semi-solids.
- In combination with a liquid fill, provides an attractive and viable dosage form, particularly for poorly soluble compounds.
- The use of hot melts is also viable with Licaps, as they may be filled at temperatures up to 70° C.

POSILOK®:

is the registered trademark for the locking system used by Qualicaps.

It ensures that the contents reach the consumer intact, and are protected at all times from external contamination.

MINICAPSULES:

The amount of material needed for testing is often very small(in mg)

Qualicap's Minicapsule(size9) provides a dependable method of delivering the material directly into animal's stomach with minimal waste & great flexibility in dosing & available in gelatin &HPMC option

CAPACITY	25 mm^3	
CAP LENGTH	4.3mm	+/-0.30mm
BODY LENGTH	7.3mm	+/-0.30mm
CAP DIAMETER	2.65mm	+/-0.10mm
BODY DIAMETER	2.40mm	+/-0.10mm
CLOSED JOINED LENGTH	8.40mm	+/-0.30mm
WEIGHT	9.5mg	+/-2mg

Some of the essential first pre-clinical tests that examine safety and pharmacokinetic factors are carried out on rodents or guinea pigs.

The amount of material needed for testing is often very small (milligram quantities).

Qualicap's Minicapsule (size 9) provides a dependable method of delivering material directly into the animal's stomach with minimal waste.

These small, size 9 capsules can be filled with small, yet precise doses.

Scientists have great flexibility in dosages because each capsule is filled individually and can be adjusted to the weight of the individual rodent.

Minicapsules are available in both gelatin and hypromellose (HPMC) options.

<u>COATING METHOD FOR SOFT GELATIN CAPSULES WITH IMPROVED STABILITY .</u>

Adding 10-90% ethanol into mixture of HPMC 20-150parts, Tween80 8.5-25vol parts, Titanium white powder 7.5-25wt parts, Talc powder 7.5-25wt parts, 2%chocolate brown solution, 7.5-25wt parts, castor oil 15-40 vol parts to obtain coating solution, regulating flow rate of coating material at 25-40°C under relative moisture of 20-60%.

It can produce soft capsules with slower aging speed.

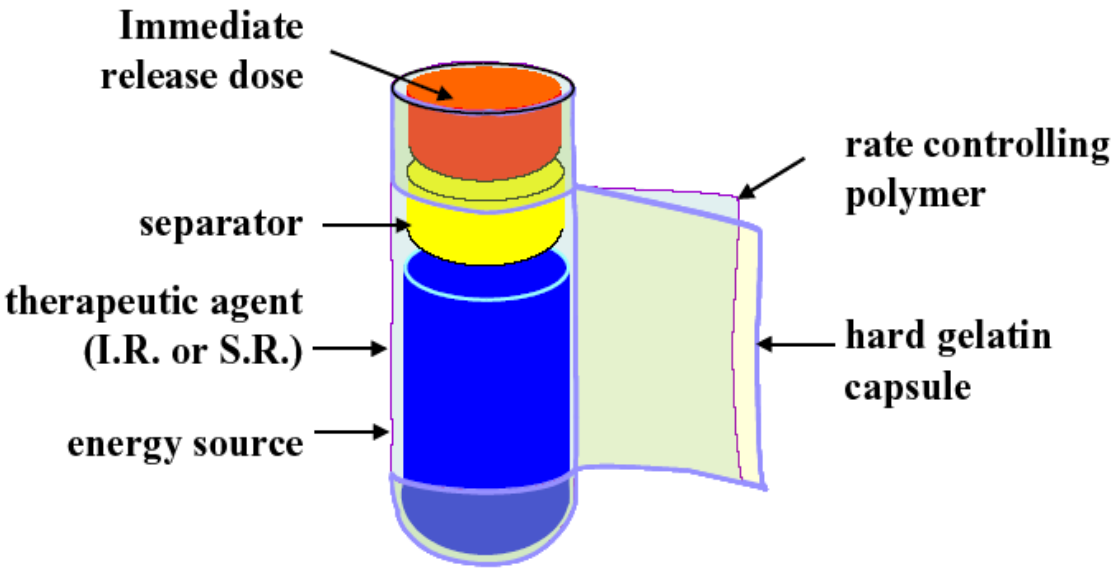
INNOVATIONS IN CAPSULE SYSTEM:

To provide modified release

- PORT CAPSULE TECHNOLOGY:
- HYDROPHILIC SANDWICH (HS) CAPSULE
- L-OROS®
- PULSINCAP
- CHEWABLE SOFT GELATIN CAPSULE ENCAPSULATING LIQUID FILL
- INNERCAP TECHNOLOGY
- GALACTICLES

PORT CAPSULE TECHNOLOGY:

eg.Pseudoephedrine delayed release



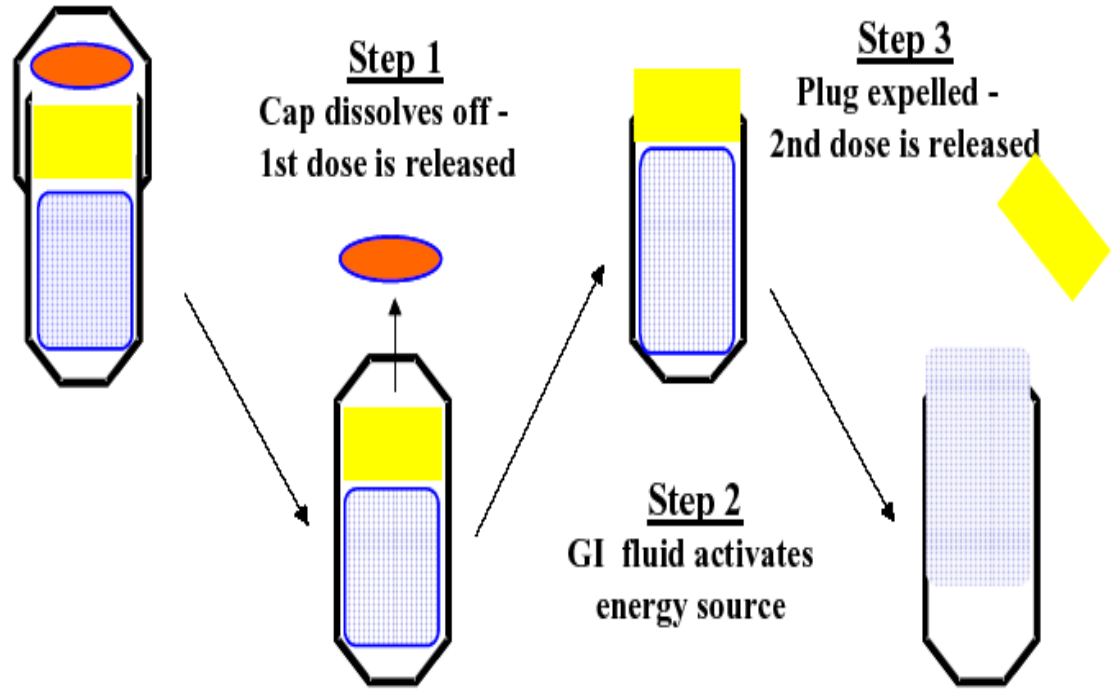
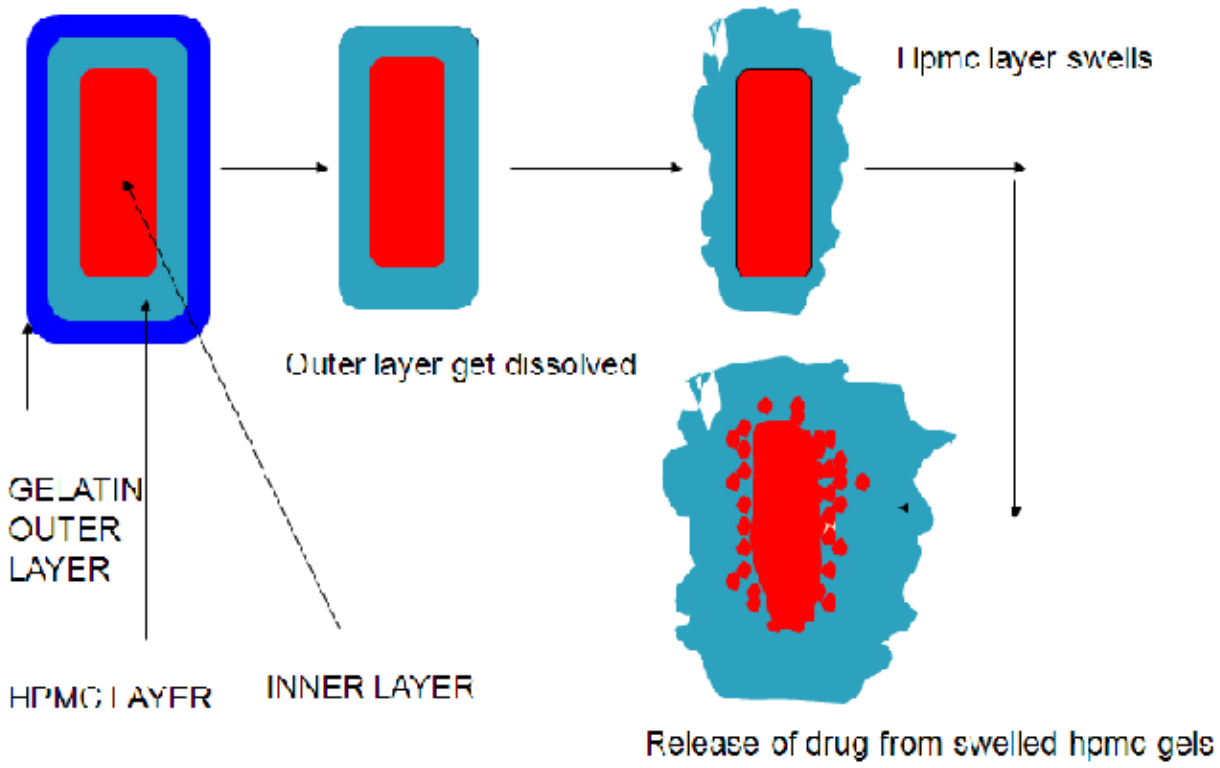


Figure 4. Drug release mechanism from the PORT Capsule.

HYDROPHILIC SANDWHICH(HS) CAPSULES:

- Simple and time delayed probe capsule
- Based on a capsule within a capsule, in which the inter capsular space was filled with a layer of hydrophilic polymer (HPMC).
- This effectively created a " Hydrophilic Sandwich " between two gelatin capsule



- When the outer capsule dissolved, the sandwich of HPMC formed a gel barrier layer that provided a time delay before fluid could enter the inner capsule and cause drug release
- The time delay was controlled by
    - Molecular weight of polymer
    - Inclusion of a soluble filler eg. Lactose

L-OROS®:for Controlled Release of Non-Aqueous Liquid Formulation

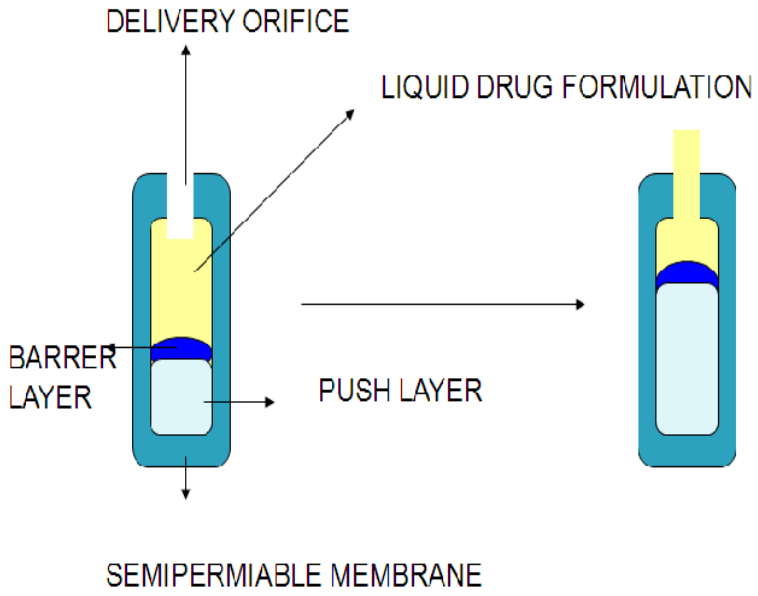
- L-OROS Hard cap
- L-OROS Soft cap
- Delayed liquid bolus delivery system
- consists of liquid drug, an osmotic engine or push layer and a semi permeable membrane coating

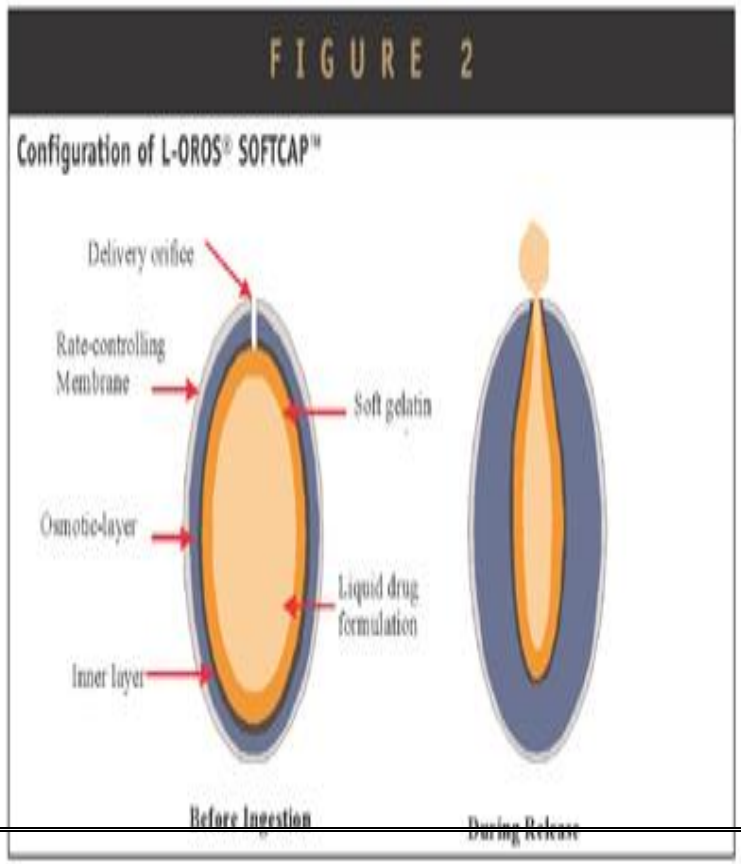
◦ **Advantages:**

- Enhanced bioavailability of class II drugs
- Uniform blood levels over specific period of time

- Reduced first pass effect
- Reduced dose
- Patient compliance
- Made of pharmaceutical acceptable excipient

1.L-OROS HARD CAP:





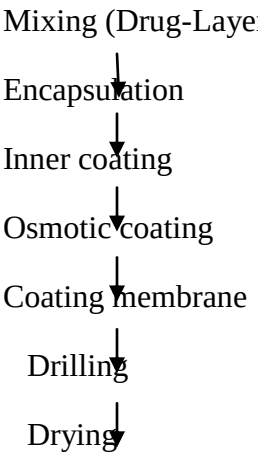
➢ The drug layer and the osmotic engine are encased in hard capsule which is surrounded by the rate controlling semi permeable membrane.

➢ A barrier layer composed of an inert substance separates the drug layer from osmotic engine.

➢ A delivery orifice is laser drilled at the opposite end of the osmotic engine providing an outlet for the drug.

2.L-OROS SOFT CAPSULES:

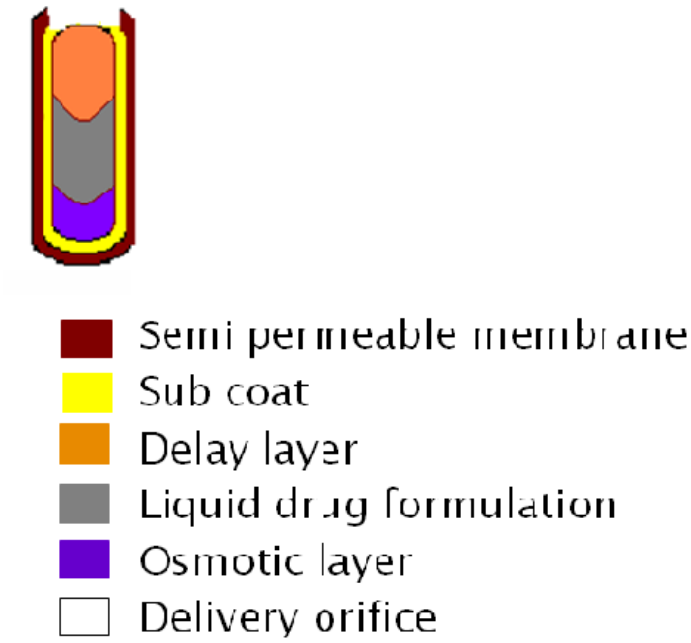
Manufacturing Flow chart:



- The liquid drug formulation is encased in soft capsule. It is in turn surrounded by a barrier layer, osmotic engine, and a semi permeable membrane in order.
- A delivery orifice in drilled through semi-permeable membrane,osmotic engine and barrier layer.
- When the osmotic engine expands it compresses the soft capsule and the drug drug formulation is pushed out through the delivery orifice.

3.DELAYED LIQUID BOLUS SYSTEM:

- Delivers the pulse of the liquid drug.
- The system consists of the placebo delay layer, a liquid drug layer, an osmotic engine all encased by a subcoat and then surrounded by semi-permeable membrane.
- The delivery orifice is drilled on the placebo layer of the system.
- When the osmotic engine expands, the placebo is released first delaying the drug release.
- Delay in drug release can be srom 1-10 hours depending on the permeability of the rate controlling membrane and the size of the placebo layer.



PULSIN CAP:

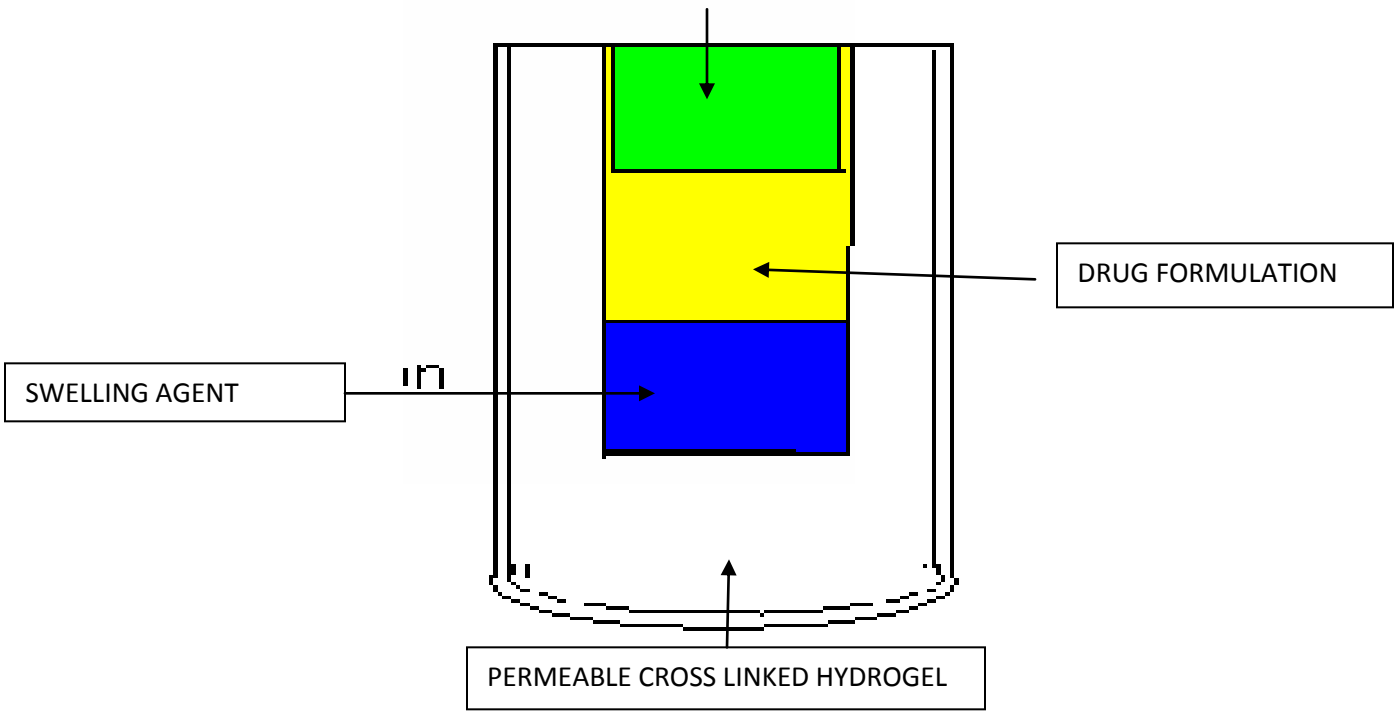
Used for pulsatile drug delivery.

In general consists of insoluble capsule body and a soluble capsule cap.

- **First concept** : separation of a plug form an insoluble capsule body.
- It comprised of a water permeable body prepared from a water-swellable hydrogel cross linked PEG polymer
- A swelling agent mixed with the drug, was filled into the internal cavity of capsule body and a plug was used to seal the contents into the internal cavity.
- Upon oral administration by the patient, cap dissolves. Water diffuses through capsule body. Swelling causes plug to move in upward direction causing drug release.
- Water diffusion into the core through semi permeable through semi-permeable membrane is controlled by:

  Hydrogel composition and Wall thickness of the capsule.

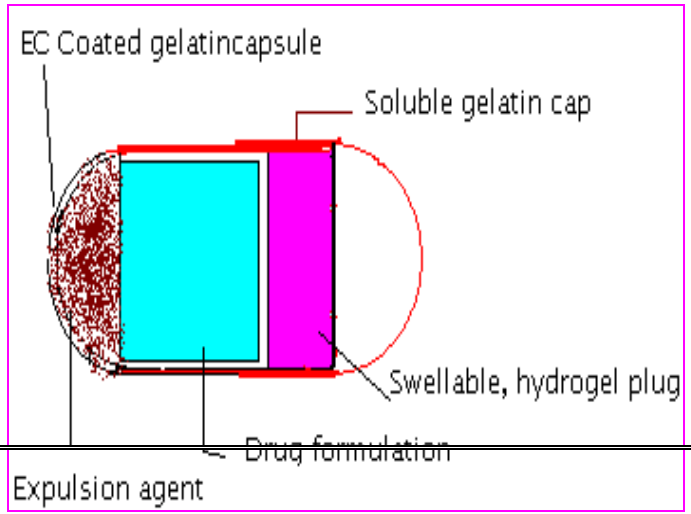
PLUG, CROSS LINKED HYDROGEL

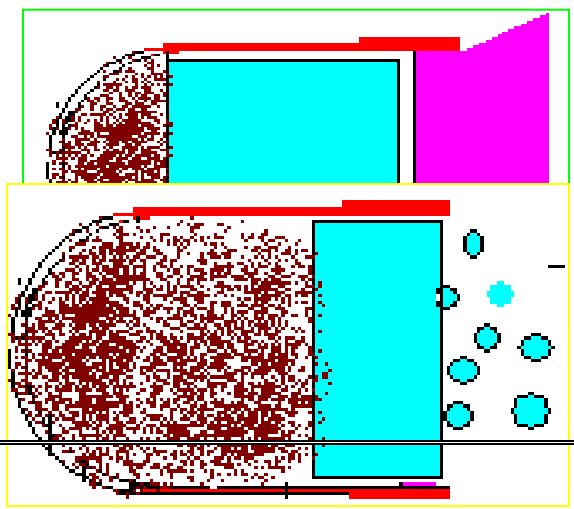


SECOND CONCEPT:

- capsule body is made of gelatin coated with ethyl cellulose.
- In the presence of fluid, the plug swelled at a controlled rate that was independent of the nature of pH of the medium.
- As the plug swells it attains frustroconical shape and it gets slowly pulled out of the capsule.
- Pulse time is controlled by:

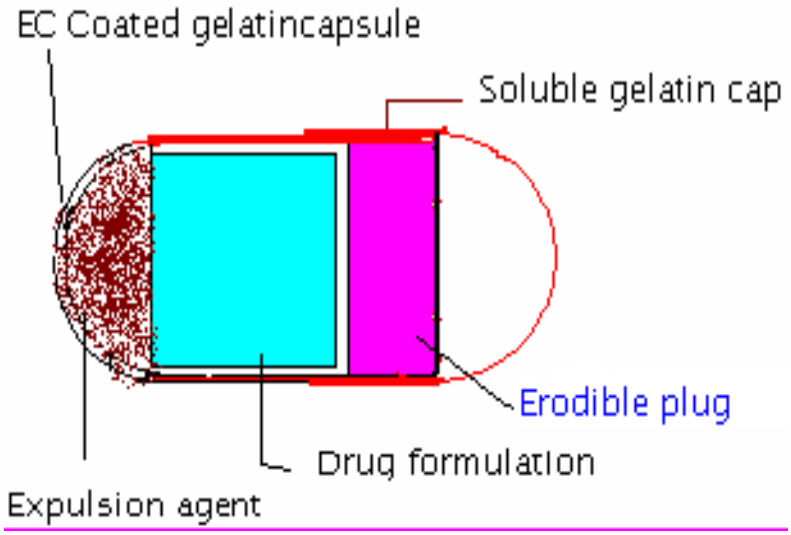
  The length of the plug and insertion distance of plug into the capsule.
- Disadvantage: not adopted for large scale manufacturing because of high cost.

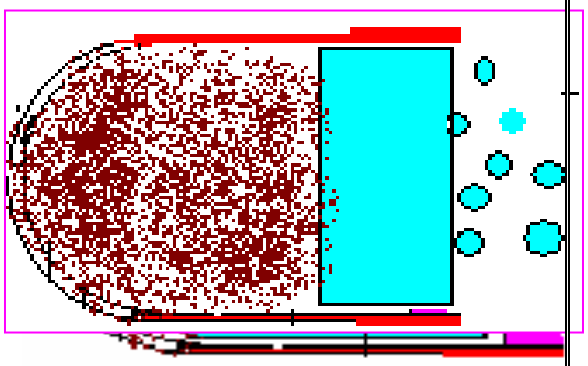




THIRD CONCEPT:

- Here in this approach in place of hydrogel plug, simple erodible compressed tablet is placed.
- This overcomes the need for the precise dimensional tolerance between capsule and plug for sliding mechanism of the plug.



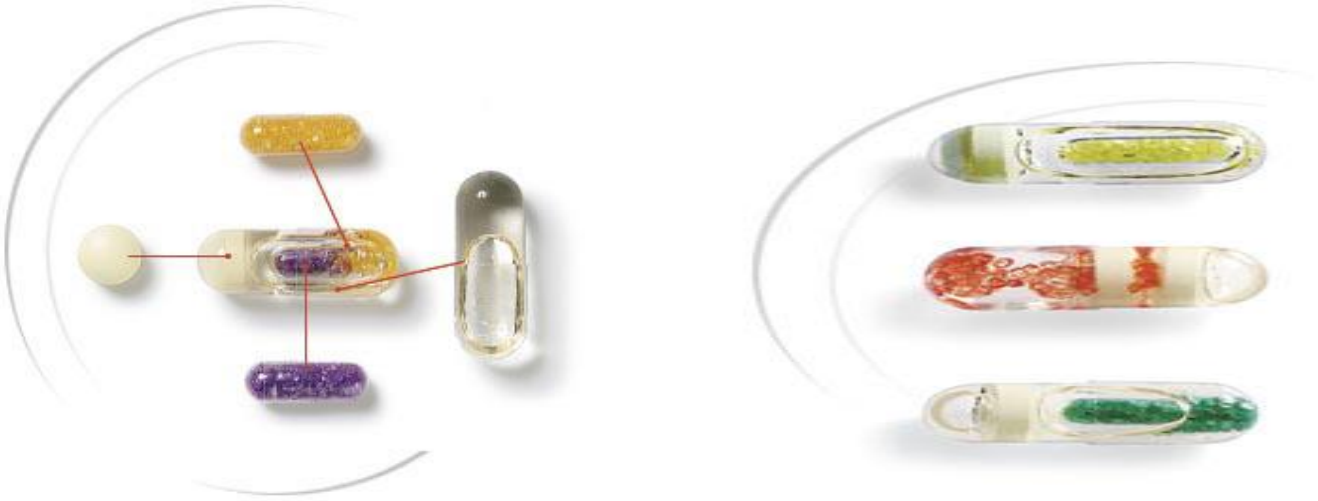


CHEWABLE SOFT GELATIN CAPSULE

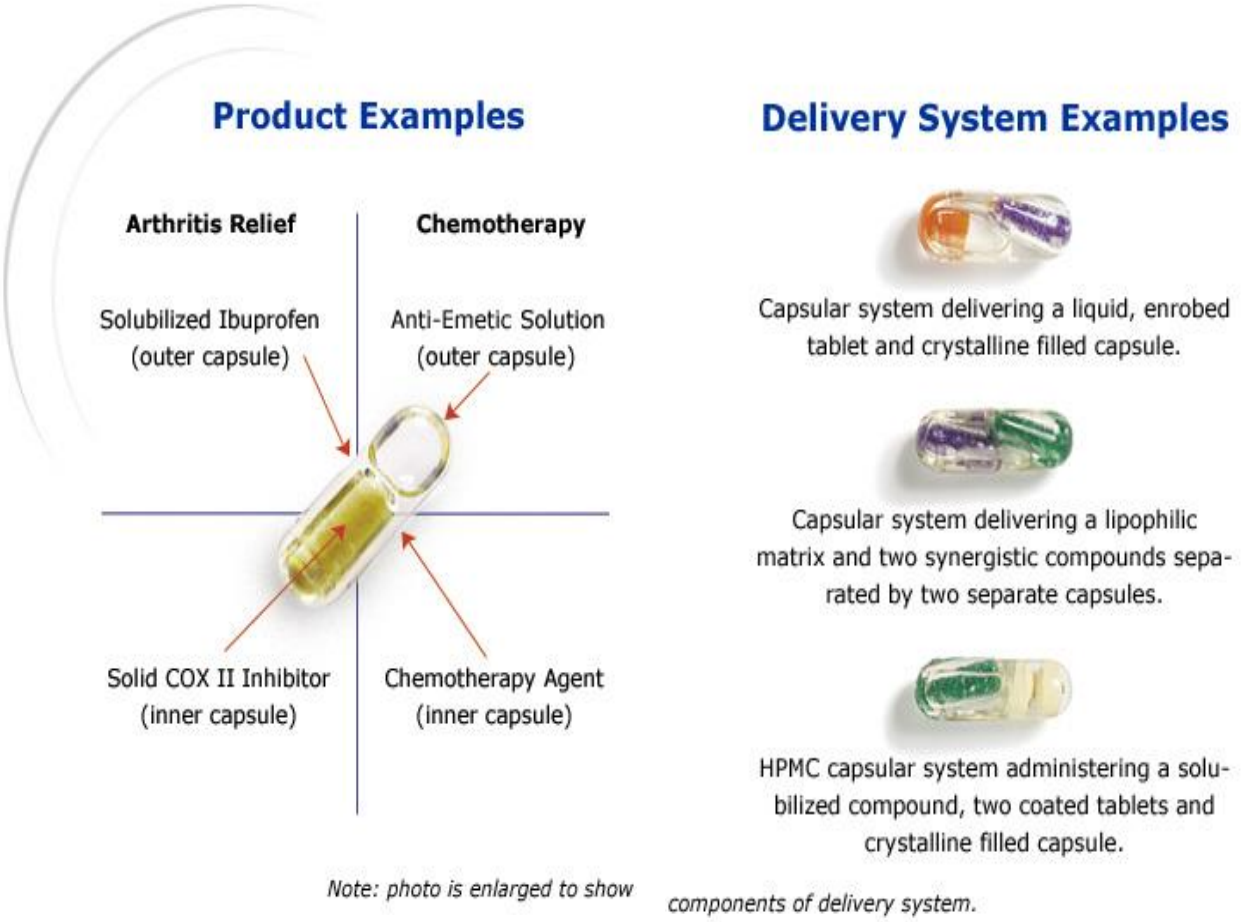
ENCAPSULATING LIQUID FILL

- Chewable SGC require mixture of gelatin having different bloom values.
- Most preferable combination ration : 3:1 to 5:1
- It contains ingredients like,
    - Low bloom gelatin
    - Medium bloom gelatin
    - Plasticizers
    - Water
    - Moisture retaining agent
    - Other

INNER CAP TECHNOLOGY:



- The combination example consists of a high potency insoluble active in a lipid emulsion, sustained release tablet and a cocktail of two crystalline active materials.
- A combination of release profiles can be incorporated in the system.
- Can deliver incompatible and compatible drugs using different physical phases.
- The combination dosage form consists of a primary HPMC capsule containing an emulsion, pH coated tablet, crystalline filled HPMC capsule and a beadlet filled gelatin capsule.



Note: photo is enlarged to show components of delivery system.

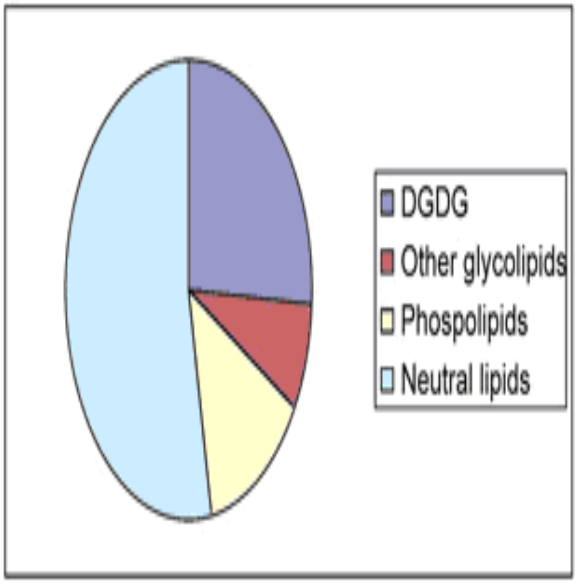
Opportunities offered by Multi – Phase Multi-compartment Capsules

- Multi -Phased Materials
- Incompatible Drugs in Single Dosage
- Capsule Shell Materials
- Multiple Release Profiles
- Single Therapies
- Multiple Therapies
- Ease of Scale-Up
- Less Excipient
- Increased Bioavailability Through Absorption
- Increased Stability

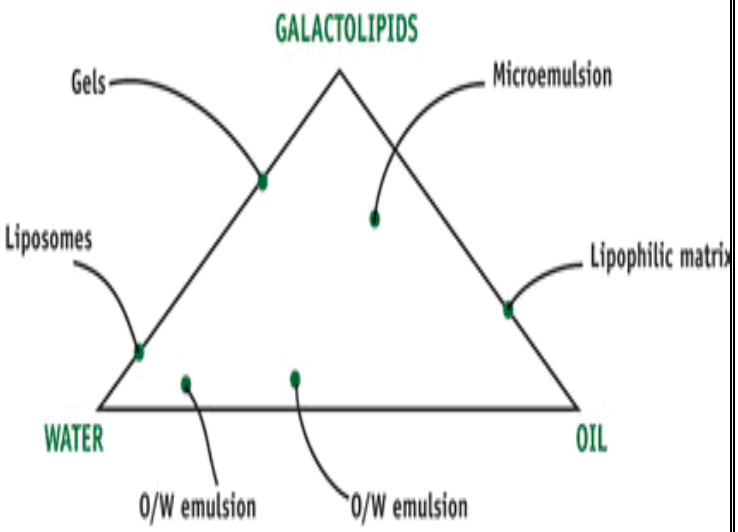
GALACTICLES™

-Oral Lipid Matrix in Liquid-Filled Softgel Capsules
-A Novel Drug Delivery System for Improved Oral Bioavailability
-The Galacticles™ Lipid Matrix consists of a mixture of galactolecithin and one or more other lipids, for example, mono-, di-, and/or tri- glycerides.

Typical composition of galactolecithin.



Schematic phase diagram, showing mixtures of galactolipids, water, and oil.



- **Potential for Improved Drug Absorption**
  improve oral bioavailability for hydrophilic and lipophilic drugs with low solubility.
- **Potential for Reduced Degradation in the GI Tract**
  reduce degradation as well as improve absorption may be especially useful for drugs, for which both low solubility and degradation in the GI tract contribute to a low oral bioavailability.
- **Tolerability & Taste**
  The fact that DGDG, in contrast to phospholipids, is uncharged makes it less prone to cause irritation
  The favorable taste of Galacticles™ formulations compared to corresponding formulations with phospholipids and synthetic surfactants
- **Safety**
  The components of Galacticles™ are natural dietary lipid components found in processed and natural foods.
  Preliminary safety studies indicate no toxic effects of oral administration

MIRISHITA JINTAN'S SEAMLESS SOFT GELATIN CAPSULES

-Perfect seamless shapes like a shining pearl.

-Principle: interfacial tension leads our unique dropping technology.

-The inner nozzle, of the concentric double nozzle, ejects core contents and the outer nozzle supplies the heated shell solution.

-through this simultaneous action, the shell solution wraps the core substances.

Extremely homogenous and very small:

No variation in size or weight.

Controllable hardness:

Hardness freely can be controlled by changing the material, water content and thickness of the shell.

Controllable shell thickness:

size can be reduced up to 30microns.

The capsule dissolves quickly. Shell can be filled with 50% or more as compared conventional soft capsule.

The shell is made of a water soluble polymer such as gelatin or agar.

CAPSULE SHELL QUALITY:

SHELL MATERIAL	ACID RESISTANCE
Agar	Disintegration under pH4
Gelatin	Dissolve by over body temp & unrelated pH
Gelatin plus Pectin	Undissolve under pH4(37°C)

SHELL MATERIAL	DISSOLVING POINT	DISSOLVING POINT IN ANHYDRATE
Gelatin	35°C<	100°C<
Agar	80°C<	100°C<
Gelatin plus thermostable Gel	100°C<	100°C<

NEWER TECHNOLOGIES(For Pulsatile Release):

SODAS® Technology:

Spheroidal Oral Drug Absorption System is Elan's multiparticulate drug delivery system. Based on the production of controlled release beads, the SODAS®Technology is characterized by its inherent flexibility, enabling the production of customized dosage forms that respond directly to individual drug candidate needs.

It can provide no of tailored drug release profiles, including immediate release of drug followed by sustained release to give rise to a fast onset of action, which is maintained for 24hours. Alternatively the opposite scenario can be achieved and additional option is pulsatile release.

Elan's SODAS® Technology is based on the production of uniform spherical beads of 1-2mm in diameter containing drug plus excipients and coated with product specific controlled release polymers.

The most recent regulatory approvals for a SODAS® based system is the once daily oral dosage forms of Avinza™ ,Ritalin®LA and Focalin®XR.

CODAS® TECHNOLOGY:

A delay of drug action may be required for different reasons. Chronotherapy is an example of when drug release may be programmed to occur after a prolonged interval following administration. Chronotherapeutic Oral Drug Absorption System(CODAS™ Technology) was developed to achieve this prolonged interval.

Verelan® PM product using this Technology is designed to begin releasing Verapamil approximately 4-5hrs post ingestion. Delay is introduced by the level of release controlling polymer applied to the drug loaded beads. The release controlling polymer is a combination of water soluble and water insoluble polymers.

As water from the GIT contacts the polymer coat beads, the water soluble polymer slowly dissolves and the drug diffuses through the resulting pores in the coating.

The water insoluble polymer continues to act as a barrier, maintaining the controlled release of the drug.

When taken at bad time, this controlled onset extended release delivery system enables a max. plasma concentration of verapamil in the morning hours, when blood pressure generally rises from its overnight low.

PRODAS® TECHNOLOGY:

Programmable Oral Drug Absorption System is multiparticulate technology; it combines the benefits of tabletting technology within a capsule.

PRODAS® system is presented as a number of minitablets combined in a hard gelatin capsule. It can be used to pre-program the release rate of a drug. It is possible to incorporate many different mini tablets, each one formulated individually and programmed to release drug at different sites within the GIT.

It is possible to incorporate mini tablets of different sizes so that high drug loading is possible.

PRODAS® technology, by incorporating mini tablets with different release rates, can display the characteristics of no of different conventional dosage forms:

-IR component will mimic conventional formulation.
-Delayed release can provide site/regional release and food resistance.
-Sustained release component provides additional controlled release/protection.

PULSYS™ TECHNOLOGY:

MiddleBrook™ Pharmaceuticals developed PULSYS™, an oral drug delivery technology that enables once daily pulsatile dosing.

PULSYS™ dosage form is a compressed tablet that contains pellets, designed to release drug at different regions in the GIT in a pulsatile manner. The dosage form is made up of multiple pellet types of varying release profiles that are combined in a proportion so as to produce a constant escalation in plasma drug levels in the early portion of the dosing interval.

The transit property of pellets enhance the overall absorption time window and offer improved bioavailability compared to tablet matrix forms.

Moxatag™ tablets contains amoxicillin and improved bactericidal action in pulsatile manner was observed as compared to standard dosing regimen.

ORBEXA® TECHNOLOGY:

Multiparticulate system that enables high drug loading and provides a formulation choice for products that require granulation.

It produces beads that are of controlled size and density and suitable for formulation as controlled release multiparticulates- using granulation, spheronization and extrusion technique.

The resultant beads can be coated with functional polymer membrane for additional release rate control and may be filled into capsules or provided in sachet form. Process allows for high drug concentration within each bead. The technology is suited for use with sensitive drugs such as proteins.

EURAND MINITABS® TECHNOLOGY:

Minitabs are tiny, approximately 2mm in diameter, cylindrical tablets. Functional membranes may be applied to the tablets to further control release rate.

It offers high drug loading, a wide range of release rate designs, and fine tuning of these release rates.

Capsules containing the Eurand Minitabs® can be opened and the contents used as a sprinkle formulation.

Banner's VersetrolTM Technology:

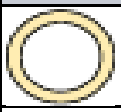
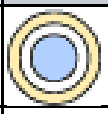
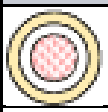
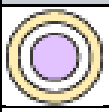
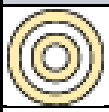
Novel innovative Technology that provides time controlled release for wide range of drug.

Drug is incorporated in lipophilic or hydrophilic matrix and that is than incorporated in soft gelatin capsule shell.

Technology is versatile because depending on physicochemical property of drug either emulsion/suspension can be developed.

For lipophilic drugs suspension formulation is preferred while for hydrophilic drugs emulsion form is utilized. By applying combination of lipophilic and hydrophilic matrices desire release profile can be achieved.

(Ref:PharmaBioWorld, October2009,Vol8,Issue 3,Page71-77)

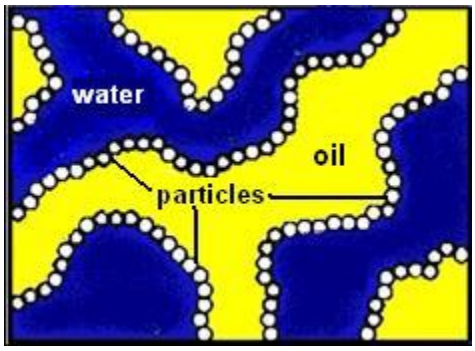
	1st Generation	2nd Generation	3rd Generation	4th Generation	5th Generation
Structure					
Concept	2 layers capsules Development of encapsulator Reduction of shell ratio	3 layers capsules Encapsulate hydrophilic substances Mass production	3 layers capsules Development of acid resistance shell Application to ethical drugs	4 layers capsules Control of release	Development of Biocapsule Incubation and cultivation in capsule
Development of function	Improve stability of content Encapsulate liquid	Mixture with products Burst impact	DDS Improvement of compliance	Deepen DDS Functional Development of 4 layers capsules	Semipermeable membrane Biotechnology
Shell Function	Solubility	Freezing resistance Heat resistance	Acid resistance Control of release	Solution in mouth + Solution in stomach Control of release	Semipermeable membrane
Content	Flavor Functional oil	Hydrophilic flavor Fruit juice exstract	Hydrophilic substance Bifidus powder	Functional oil	Lactobacillus Yeast DNA. cell
Application	Chewing gum Health food Tooth paste Instant noodle	Crystal Dew Capsule JINTAN Ice cream	Bifina Constipation OTC Solmiran	Twin clean Plum Freshener	Biotechnology

Bijel Capsules: Co-release Micro-gel

Colloid scientists at the University of Edinburgh have invented a new generic route to gel capsule formulation, involving particles suspended in fluid-bicontinuous mixture of two solvents.

These capsules have highly tunable properties (eg, shear modulus and release rate), which can be selected for different applications, such as personal care, foodstuffs, and home care. A key feature of these capsules is the internal architecture: they have inter-penetrating domains of immiscible fluids (bicontinuity).

The bijel capsules are made of two fluids and hence they are both a gel and an emulsion. The water and oil domains inside the capsules can be used to deliver chemically different active ingredients. The capsules can be designed to release or mix the active ingredients in response to a specific external stimulus.



Cross-linked DNA capsules templated on porous calcium carbonate microparticles:

To prepare hollow microcapsules composed of native DNA, we developed a templating method using porous calcium carbonate microparticles as sacrificial templates. At first, DNA was adsorbed onto calcium carbonate microparticles, and then the adsorbed DNA was covalently cross-linked with each other by using ethylene glycol diglycidyl ether. After the dissolution of the templates, the resultant DNA capsules ranged from 1.5 to 8 μm in diameter, according to ionic strength. The low cross-linked and highly cross-linked DNA capsules exhibited enzymatic degradability and permeability that was dependent on the molecular weight of macromolecular solutes, respectively. This method has the potential to be used for the preparation of various single-component polymer capsules.