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Review

Emerging Techniques In Drug Delivery Systems

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Abstract

Organogel are semi- soild system in which a three - dimensional network of self assembled, interlaced gelator fibres immobilizers an organic liquid phase. Unfortunately, the toxicity of the selected organic solvents has impeded their usage as medication delivery methods in the past.

Although transdermal drug delivery systems (DDS) offer numerous benefits for patients including the avoidance of both gastric irritation and first pass metabolism effect, as well as improved patient compliance, only active ingredients. The hard gelatin capsules is the most versatile of all dosage forms capsule are soild dosage contains two pieces as it consists of two pieces is small cylinders closed. The administration of liquid and soild drugs enclosed hard gelatin capsule one of the most frequent utilzed dosage forms.

The study investigates kneaf core drying uniformity in a tray dryer through computational fluid dynamics simulation. However the greatest draw back of the tray dryer is uneven drying because of poor air flow distribution in the drying chamber implementing the property design of tray dryer system may eliminate or reduce non uniformity of drying and increase dryer efficiency.

Keywords: Drug Delivery system, Organogel, Physiochemical.

INTRODUCTION

PREPARATION OF ORGANOGEL

Organogel formulation is often accomplished by dissolving an organogelator in a hot, apolar phase, followed by a chilling process that results in gelation. Organogels are made using the following processes, which are based on their inherent nature.[24]

Chemical Organogels

Crosslinked copolymeric organogel are made via chemical techniques including copolymerization reactions. Along with monomers, crosslinkers like N, N-methylene bisacrylamide, or polyethylene glycol diacrylate can be utilized. Under stirring at a moderate temperature (60-70°C), they form covalent connections

between organogelator molecules, trapping the solvent phase. These settings allow polymerization events to begin, resulting in the creation of gels at critical gelator concentrations (CGC). Bera et al., for example, found that increasing the crosslinker content to more than 2% w/v reduced the inflammation of N-tertiary butyl acrylamide- and acrylic acid-based copolymer organogels are shown in Figure1.[25]

Physical Organogels

The heat-cool approach is most commonly used to make physical organogels. Gelator molecules are dissolved in the organic solvent in this example. The liquid phase is then mechanically stirred with the help of rotor-stator homogenizers and heated to 60-80°C, even 100°C for 1,3:2,4-di-Obenzylidene-D-sorbitol organogels until a clear solution is formed.[27] The heated solution is subsequently cooled to ambient temperature, sometimes using sonication, to achieve homogenous dispersions in a couple of minutes. The physical organogels are mostly fluid-filled matrix or solid fiber matrix type and their method of preparation is shown in Figure 1.

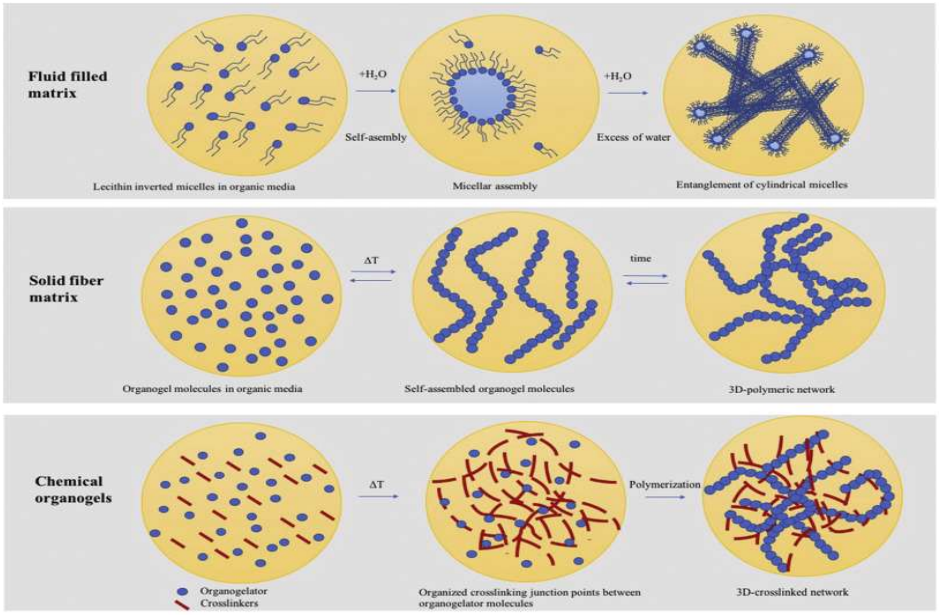


Fig 1: Preparation methods influencing Organogel Structure

Characterization of Organogel

To confirm the stability and effectiveness of organogel, characterization of organogel through various methodologies and techniques is very important. Various properties such as gelator-co-gelator interactions, the gelator-polar/apolar solvent interactions, drug interactions with gel components, and the gelatorassemblies may be investigated during the characterization of organogels.

Physiochemical Properties

Structural features can influence the physicochemical properties of the organogel. Structural elucidation is an efficient characterization methodology for organogels. Different types of spectroscopy and microscopy technique are used for the determination of the 3-D structure of the organogel, morphology, and specific interactions. Spectroscopy techniques include nuclear magnetic resonance, Fourier-transform infrared spectroscopy, and magnetic resonance imaging, etc. Microscopy techniques include transmission electron microscopy, scanning electron microscopy, atomic force microscopy, polarized light microscopy, etc. Microscopy analysis is the simplest characterization method to analyze the structural features of organogel.

Advantages of Organogels[5,6]

- Organogels are more stable than other forms of gels.
- Preparation is simple.Avoid the first-pass metabolism.
- Thermodynamically stable.
- Organogels are moisture insensitive.
- Inexpensive due to less number of ingredients.
- Improved the penetration of the drug through the skin.

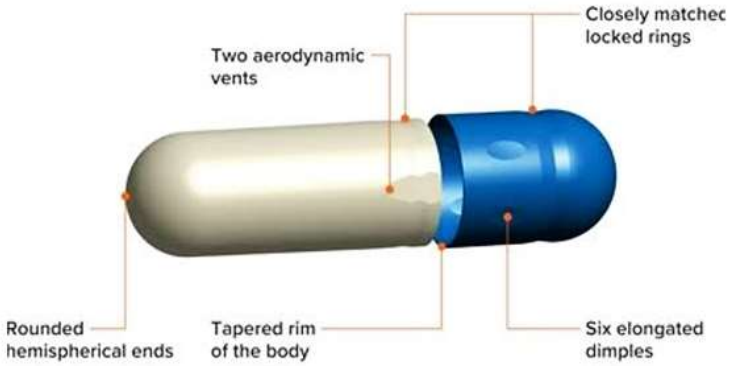
Disadvantages of Organogels[5,6]

- Requires an appropriate storage environment.
- Drugs that irritate or sensitize the skin are not suited for this method.
- There will be no gelling if there is an impurity present.
- The most expensive ingredient is lecithin, which is not widely accessible.

LIQUI CAPS

Capsule is the most versatile of all dosage forms. Capsules are solid dosage forms in which one or more medicinal and inert ingredients are enclosed in a small shell or container usually made of gelatin.

There are two types of capsules, "hard" and "soft". The hard capsule is also called "two piece" as it consists of two pieces in the form of small cylinders closed at one end, the shorter piece is called the "cap" which fits over the open end of the longer piece, called the "body". The soft gelatin capsule is also called as "one piece". Capsules are available in many sizes to provide dosing flexibility. Unpleasant drug tastes and odors can be masked by the tasteless gelatin shell. The administration of liquid and solid drugs enclosed in hard gelatin capsules is one of the most frequently utilized dosage forms.[7]



LIQUIDS IN HARD GELATIN CAPSULES

Liquids can be prepared in hard gelatin capsules if the gelatin is not soluble in the liquid to be encapsulated; alcoholic solutions and fixed and volatile oils work well. It may be necessary to determine the solubility of gelatin in the liquid by experimentation. The liquid can be measured accurately using a pipette (micropipet) or a calibrated dropper and dropped into the gelatin base, taking care not to touch the opening. The gelatin caps can be touched, open end down, on a moist towel to soften the gelatin at the opening of the caps or a cotton swab dipped in warm water can rubbed around the edge of the capsule cap to soften. The cap is placed over the base containing the liquid with a slight twist and the softened edge of the cap should form a seal with the base to prevent leakage. Prior to packaging, these capsules should be placed on a clean, dry sheet of paper and observed for leakage. Another method of sealing makes use of a warm gelatin solution that is painted around the capsules and the inside of the caps prior to placing on the base.[6,9]

Advantages of Capsules

- Capsules mask the taste and odor of unpleasant drugs and can be easily administered.
- They are attractive in appearance.
- They are slippery when moist and, hence, easy to swallow with a draught of water.
- As compared to tablets less adjuncts are required.
- The shells are physiologically inert and easily and quickly digested in the gastrointestinal tract.
- They are economical.
- They are easy to handle and carry.
- The shells can be opacified (with titanium dioxide) or colored, to give protection from light.

Disadvantages of Capsules

- The drugs which are hygroscopic absorb water from the capsule shell making it brittle and hence are not suitable for filling into capsules.
- The concentrated solutions which require previous dilution are unsuitable for capsules because if administered as such lead to irritation of stomach.

Methodology of hard gelatin capsules

Steps involved in making hard gelatin capsules are listed below.

1) **Dipping:** Pairs of the stainless-steel pins are dipped into the dipping solution to simultaneously form the caps and bodies. The dipping solution is maintained at a temperature of about 500C in a heated, jacketed dipping pan.
2) **Spinning:** The pins are rotated to distribute the gelatin over the pins uniformly and to avoid the formation of a bead at the capsule ends.
3) **Drying:** The gelatin is dried by a blast of cool air to form a hard shells. The pins are moved through a series of air drying kilns to remove water.
4) **Stripping:** A series of bronze jaws strip the cap and body portions of the capsules from the pins.
5) **Trimming and joining:** The stripped cap and body portions are trimmed to the required length by stationary knives. After trimming to the right length, the cap and body portion are joined and ejected from the machine.[6,9]
6) **Polishing:**
   a) Pan Polishing: Acela-cota pan is used to dust and polish.
   b) Cloth Dusting: Capsules are rubbed with cloth.
   c) Brushing: Capsules are feed under soft rotating brush.

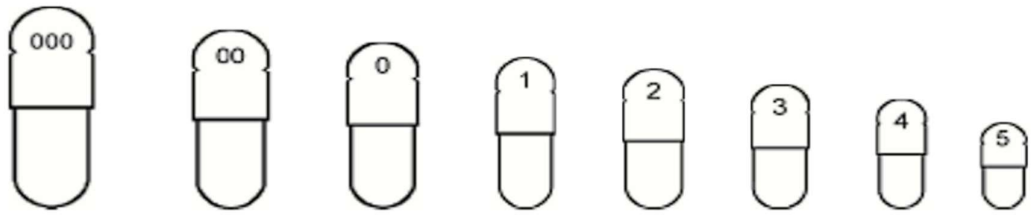
Capsule shell filling

Hand Operated Hard Gelatin Capsule Filling Machines

hand operated and electrically operated machines are in practice for filling the capsules but for small and quick dispensing hand operated machines are quite economical. A hand operated gelatin capsule filling machine consists of the following parts and is shown in figure.

1. A bed with 200-300 holes.
2. A capsule loading tray
3. A powder tray.
4. A pin plate having 200 or 300 pins corresponding to the number of holes in the bed and capsule loading tray.
5. A lever.
6. A handle.
7. A plate fitted with rubber top.[8]

Table 1: Size of hard gelatin capsules -Capsule size chart



PACKAGING AND STORAGE OF CAPSULES

Capsules should be packed in a well-closed glass or plastic containers and stored in a cool place. These type of containers have advantage over cardboard boxes that they are more convenient to handle and transport and protect the capsules from moisture and dust. To prevent the capsules from rattling a tuft of cotton is placed over and under the capsules in the vials. In vials containing very hygroscopic capsules a packet-containing desiccant like silica gel or anhydrous calcium chloride may be placed to prevent the absorption of excessive moisture by the capsules. Now a days capsules are strip packaged which provide sanitary handling of medicines, ease in counting and identification.

Empty gelatin capsules should be stored at room temperature at constant humidity. High humidity may cause softening of the capsules and low humidity may cause drying and cracking of the capsules. Storage of capsules in glass containers will provide protection not only from extreme humidity but also from dust. Storage of filled capsules is dependent on the characteristics of the drugs they contain. Semisolid filled hard gelatin capsules should be stored away from excessive heat, which may cause a softening or melting of the contents.[11]

Microneedle arrays

The application of various chemical agents on the skin dates back thousands of years, when they were applied to treat diseases, protect the skin, or for cosmetic reasons. The ancient Greeks made balm from a mixture of water, olive oil, and lead (II) oxide, whereby olive oil and lead (II) oxide had an occlusive and astringent ect, respectively. However, the skin was considered as an impermeable membrane until 1893, when Bourget proved that the topical application of salicylic acid could treat acute rheumatoid arthritis.[3]

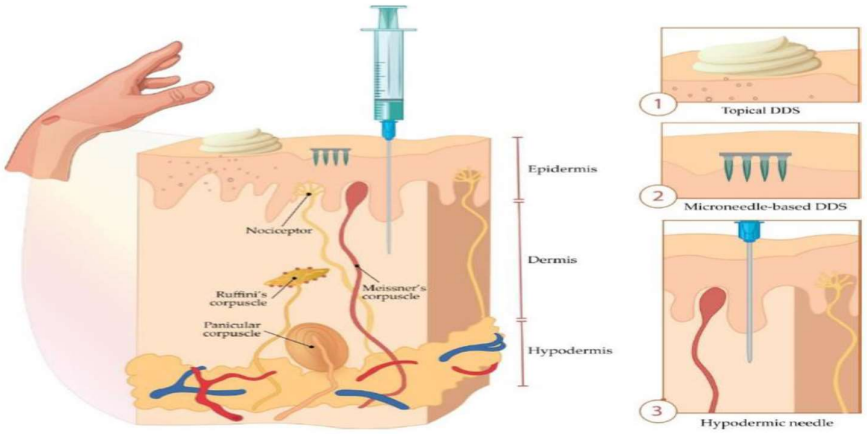


Figure 1. Comparison of drug delivery systems (DDS) based on (1) the conventional topical formulation, (2) microneedles (MNs), and (3) hypodermal injection.

At the beginning of the 20th century, lipophilic agents were discovered to increase skin permeability, and usingWolf's tape stripping technique, Blank concluded that the stratum corneum (SC) represents the main barrier for the penetration and permeation of active pharmaceutical ingredients (APIs). Skin, as a drug delivery route to the systemic circulation, was neither commercially nor scientifically employed until 1954, when it was shown that 2% nitroglycerin ointment could control angina pectoris. Therefore, this ointment was the first commercial preparation formulated for the transdermal delivery of API into the systemic circulation.

Classification of micro needles

There are several ways to classify MNs. Some authors divide them into solid and hollow MNs and include coated, uncoated, and dissolving MNs in the category of solid ones. Others divide them according to the production method into "in-plane MNs" (microneedle shafts oriented parallel to the base substrate) and "out-of-plane MNs" (microneedle shafts bent at 90 to the base substrate). The most common categorisation is into five types.

- **hollow MNs**—used for the injection of liquid drug formulations through the MN bores into the skin;
- **solid MNs**—used for the pretreatment of skin before administration of APIs from the external reservoir;
- **coated solid MNs**—used for the continuous dissolution of APIs in the skin, as the drug is coated on the MN shaft and tips;
- **dissolving MNs**—that dissolve completely in the skin and thus release drugs or vaccine incorporated into the MN matrix; and
- **hydrogel MNs**—that swell up upon administration and API release from the patch through swollen MNs.[36]

Methodology of microneedles

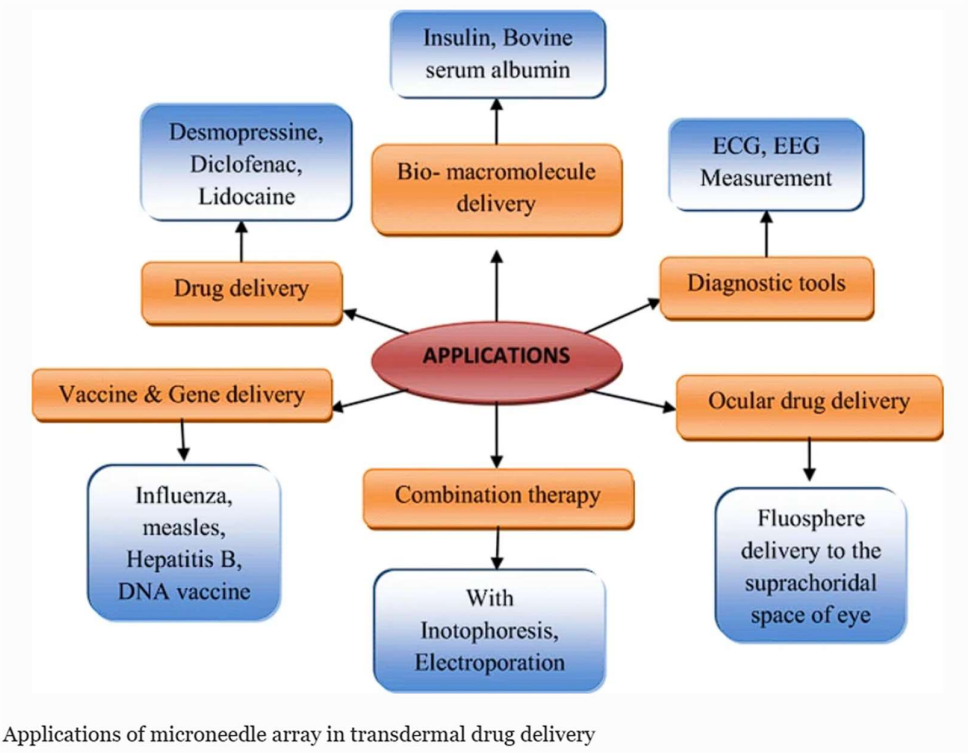
The advent of microfabrication manufacturing technology in recent decades has enabled the development of MNs in research laboratories and pharmaceutical companies. Therefore, it is necessary to select the most suitable materials for MN production based on the following criteria:

- gentle manufacturing without damaging sensitive and unstable molecules;
- controlled or immediate drug release;
- and sufficient mechanical strength for skin penetration.

The first solid MNs were made of silicon, as industrial high-precision microelectronics tools and silicone flexibility enabled the production of MNs. However, their main disadvantage is the breakage of the silicon MN due to their brittle nature. Nowadays, MNs come in a variety of shapes and sizes, as well as materials, including stainless steel, titanium, nickel-iron, glass, and ceramics. Metal MNs have sufficient mechanical strength to penetrate the skin, but their disadvantage is that they generate potential biological waste. Interestingly, nitinol is used in vascular surgery due to its advantages in terms of elasticity, shape-memory capability, and

biocompatibility. However, polymeric MNs have better solubility and usage in case of the tip breaking. Water-soluble polymers and engineering plastics such as CMC, poly (glycolic acid) (PGA), polylactic-co-glycolic acid (PLGA), poly (vinyl alcohol) (PVA), poly (vinylpyrrolidone) (PVP), polylactic acid (PLA), chondroitin sulfate, and polycarbonate are employed forMNproduction, whereas dissolving MNs are composed of sugars such as maltose, dextran, or galactose.[79,80]

Applications of microneedle array



Applications of microneedle array in transdermal drug delivery

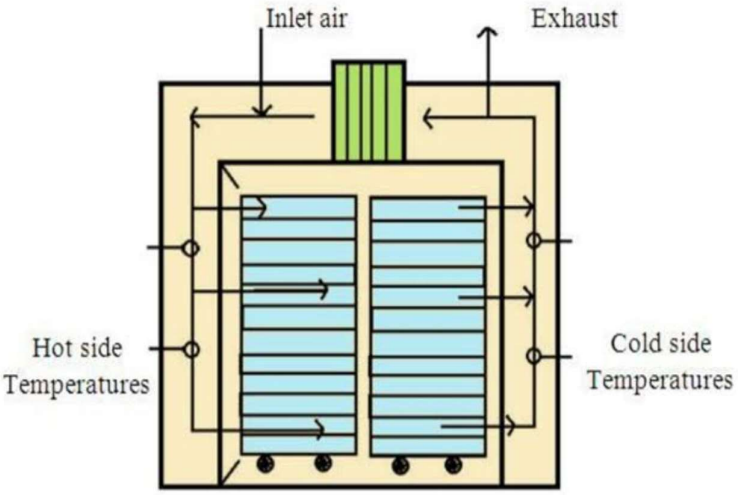
Dry solving

Tray Dryer

Tray drying is a batch process used to dry materials that are liquid or wet cake. Tray drying works well for material that requires more gentle processing or cannot be atomized in an airstream due to viscosity. This dryer is well utilized for drying of wet products like crude drugs, chemicals, powders, or granules, etc. It is the most conventional dryer, used very widely and still being used where the moisture content is higher and where the product has to be dried at a low temperature for long hours.[5]

Construction of Tray Dryer

Tray dryer can be electrically or steam heated. It consists of any number of trays that varies with customer requirement. It is fabricated out of a rigid angle iron frame with double walled panels insulated with the best quality compressed fiberglass and with a rigid door fitted with strong hinges and the best-chosen locking system. There may be a facility to circulate hot air such as fans. A control panel is fixed in the front of the oven to facilitate easy operation. It has a large functional space and is made of mild steel and in good finishing outside with synthetic enamel color and inside painted with heat resistant paint to resist temperature up to 300 ºC.[7]



Working of Tray Dryer

Tray dryer is widely used in the pharmaceutical industries. The material to be dried is placed on the trays. The heat in the dryer is produced by the heater along a side or at base. Other than the hot air generated by the oven, the other method is to employ radiator coils that use steam for heat circulation. During the heating process the material to be dried is spread out on the trays. The heated air is directed to flow in a circulation form. It flows over the material in the trays in a controlled flow. Trays can have a solid, perforated or wire mesh base. A paper lining could be used to reduce chances of contamination through contact with the tray.[16]

The efficiency of the dryer depends on recirculation of the hot air. Apart from a regular supply and presence of heated air, it also depends on supply of fresh air. The fresh air is combined with the heated air in fixed proportion for an efficient performance. Such regulated drying is important to ensure uniform drying in the dryer at the bottom as well as at the top. Apart from the double-walled construction insulation is achieved by heating coils.

Advantages[18]

- It is operated on batch mode so each batch can be handled as a separate entity.
- It is energy efficient dryer as it consumes less energy.
- It's simple to use and clean.
- Tray dryer is available in different sizes thus capital cost can be controlled.
- Chamber walls are heated externally thus prevents condensation.

Disadvantages[18]

- As it is operated at low to intermediate temperatures the process is time-consuming.
- Only a fraction of the solid particles are directly exposed.
- Heat transfer and mass transfer are comparatively inefficient.
- It provides tendency to over-dry contents in the lower trays.
- The operation is long during cycle (5 to 45 h per batch) and expensive to operate due to high labour requirement for loading and unloading.
- Plastic substances can also be dried using this dryer.

Applications of Tray Dryer

- Tray dryer has industrial applications such as in chemical and pharmaceuticals.
- Sticky materials, granular mass or crystalline materials, precipitates, and paste can be dried in a tray dryer.
- It has been used in agricultural drying because of its simple design and capability to dry products at high volume.[19]

CONCLUSION

The physiochemically features of organo-gels play critical role in their production and stability, as has been well documented in the literature. Therefore, some of the Microneedles devices have reached the commercial

market. MN- based transdermal drug delivery play significant role in modern health care system in the future and sucess of these minimally - invasive devices would also open up wide range of therapeutic opportunities for buccal, oral, vaginal rectal, and ocular drug delivery.

The solar - assisted soild desiccant dryer was performed under average solar radiation simulation was used to predict air flow distribution in the drting chamber. The hard gelatin capsule in developing and manufacturing medicines has increased considerably electronic and magnetic capsule drug delivery enables the conventional capsule for novel therapies locallized drug delivery.

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