Solvent Evaporation as an Efficient Microencapsulating Technique for Taste Masking in Fast Disintegrating Oral Tablets

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ABSTRACT
Microencapsulation is an extensively used technology of present era, that has been applied to various fields like pharmaceutical industry, agriculture, cosmetics and food technology. With the help of which liquid or solid material can be encapsulated inside a polymeric coating film for various reasons such as taste masking, control release and enhancing stability and etc. Microencapsulation can be achieved with different approaches and methods but one of the popular and frequently used feasible method is Solvent evaporation. Solvent evaporation is based on emulsification, solvent evaporation and extraction of microspheres, recently many variations have been made in this technology to improve the yield and properties of microspheres. Solvent evaporation has been widely used in microencapsulating for different purposes one of which is taste masking of bitter drugs in fast disintegrating oral tablets, for pediatric and geriatric use. FDTs are center of attraction due to their merits and feasibility of use for people with problem of dysphagia at the same time, it can also improve bioavailability and time of action of drugs. The main focus of current review is use of solvent evaporation technique for taste masking of bitter drugs in production of fast disintegrating oral tablets. In this review, we will summarize uses, novelties and variations in Solvent Evaporation technique, preparation technique, materials used, merits and demerits of this method over other microencapsulation method in taste masking.

Keywords: Microencapsulation, Solvent Evaporation, FDTs, extraction, microspheres

1. Introduction
In last decade many novelties and development has been shown up in field of pharmaceutics, one of which is encapsulation of drugs that can be done on nano and micro scale. However, Microencapsulation is a technique that has been used for several decades, it’s a term that present microspheres with a size of 1µm or less, liquid or solid particles encapsulated with a secure external layer that offers merits such as control drug release, better drug efficacy, better bioavailability, better drug stability, and low toxicity. [1] Till now different techniques have been used for microencapsulation such as solvent evaporation, spray drying, polymerization, coacervation, and phase separation and most of them have been applied in production of fast disintegrating oral tablets, [2] for example oxalic acid was microencapsulated by coacervation method [3] also metformin hydrochloride was microencapsulated with same approach of coacervation as sited in [4], taste masked ofloxacin microspheres by solvent evaporation,[5] microencapsulation of antioxidant compounds from black berry [6] microencapsulation of carotenoids [7], moreover taste masked microspheres of famotidine that were applied in preparation of famotidine orally disintegrating tablets, reported by Jiachen Xu [8] were also prepared by spray drying approach, trioctylmethylammonium chloride (TOMAC) microencapsulation was reported to be performed by suspension polymerization technique as narrated by [9].

2. Solvent evaporation technique
Solvent evaporation is a frequently used in fabrication of micro and nanoparticles, moreover it has been used in fabrication of hydrophobic lipid
nanostructures, that is based on preparation of an emulsion by agitating and later evaporation of internal phase. Drug to be encapsulated is dissolved or dispersed in a polymeric solution that was dissolved in a volatile organic solvent to form a suspension, an emulsion or a solution. Now this organic phase is further emulsified with the help of emulsifying agent in a non-solubilizing polymer vehicle, that isn’t miscible with the organic solvent in which polymer was dissolved. After stabilization of emulsion, emulsion is agitated until the solvent evaporates, the volatile solvent will diffuse through the continuous phase resulting in solid microspheres that are extracted by filtration or centrifugation and are washed and dried.

**Figure 1. Solvent Evaporation Technique**

3. Types of solvent evaporation

Solvent evaporation technique has two types, and is further divided into various types as given below and the examples of drugs microencapsulated by by these methods are shown in table 1;

i. Solvent Evaporation (Emulsification-Evaporation)
   a. O/W emulsions
   b. Multiple Emulsions w/o/w
   c. O/O non aqueous Emulsions,
   d. O/W dispersion technique

ii. Solvent Extraction (Emulsification-Extraction)

| Drug                  | SE Technique | Ref. |
|-----------------------|--------------|------|
| Oxalic Acid           | o/o          | [10] |
| Antisense oligonucleotides | o/o/o      | [11] |
| Vaccine antigens      | o/w          | [12] |

4. Why are drugs encapsulated?

Encapsulation of drugs are done for different purposes, such as;

a. Fabrication of sustained drug release formulation,

b. Utilized for taste masking and odor masking of drugs to improve organoleptic properties of drug,

c. Drug protection from environmental factors for instance light, moisture, enzymes, and oxygen,

d. Biodegradation of drug molecules in body,

e. To prevent drug incompatibilities,

f. To change the site of absorption [15].

The purpose for taste masking of bitter drugs with help of solvent evaporation microencapsulation technique, is our main target to study in this review. One of the major drawback of solvent evaporation is use of organic solvents to solubilize polymers that can be toxic and hazardous to health such as dichloromethane, ethyl acetate and etc. It has many merits too such as reproducibility, efficient, economic, and needs less operating skills, on the basis of these merits it’s long been used for different purposes mentioned above. Eudragit has been frequently applied for taste masking as its insoluble in mouth pH but soluble in stomach thus it covers the core material with shell and provides it taste masking properties. From the above introduction it’s obvious that solvent evaporation is a very essential and developing approach for microencapsulation, and is one of the currently applied technique in pharmaceutics, thus here we sought to review the use of solvent evaporation technique in taste masking in fabricating Fast Dissolving Oral Tablets.

5. Application of solvent evaporation technique in Taste masking

Solvent evaporation is a frequently applied tool for microencapsulation of different drug
molecules, bio molecules, proteins peptides, bitter drug molecules and even for encapsulation of food products and pesticides. Solvent evaporation method is a reproducible method that has been applied for microencapsulation of both solids and liquids, the size of microspheres produced by this way is 600-5000, process of microencapsulation requires less time and less operating skills. It’s a method that has been efficiently used in taste masking of bitter drugs, by creating a physical barrier or coating around the drug particles, that would eventually hinder the dissolution of drug in mouth [16]. Capsaicin that is the substance that gives bitterness to chilli’s, and is used in different spies. Capsaicin has a pungent odor and a very hot tasted, at the same time it has very good anti-inflammatory effects, also is anti-microbial. However, the odor is very uncomfortable and unbearable patients, thus microencapsulation has been applied to cover these properties. Capsaicin was efficiently microencapsulated inside the shell of polylactic acid (PLA) with help of solvent evaporation method. Capsacin was dissolved in the poly lactide acid solution and later into PV A- aqueous phase. DCM used as organic solvent was then removed by solvent evaporation [17]. Polymeric microcapsules of actamiprid a water soluble compound that is used as a pesticide, were produced with help of solvent evaporation method [18]. Cefpodoxime Proxetil microspheres were produced by a novel technique, called the emulsion solvent diffusion method where the water-insoluble drug and polymer are dissolved in a suitable solvent system mixed .The drug solution is poured slowly into an aqueous medium containing surfactant under constant stirring, and the o/w emulsion droplets are formed as soon as they meet each other. The droplets solidify gradually while the good solvent diffuses out of the droplets into the aqueous medium and finally forms microspheres. The process was reported to have satisfactory percentage yield of 78-86.87% [19]. Microspheres of roxithromycin with eudragit S100 and silica were prepared by emulsion solvent diffusion method to mask the bitter taste of roxithromycin. Where surprisingly the taste masking improved with decrease in ratio and 1:1 ration of Eudragit S100 to roxithromycin masked the bitter taste very well, however as Eudragit S100 dissolves in pH above 7 thus its dissolution was limited and remained intact in stomach for a very long time that in result will delay the start of drug action [20].

6. Taste masking of fast disintegrating tablets

Generally microencapsulation techniques have great merits such as effective and consistent coating, a wide range of particle size, enhanced stability of drug, that are later blended with other excipients and compressed into oro-dispersible tablets. As, FDTs disintegrate in mouth cavity the grittiness of particles can discomfort the patient that usually happens if drug is microencapsulated by fluidized bed dryer or spray drying, however particles of drugs microencapsulated by solvent evaporation tend to be less gritty and have a better feel in mouth. In order to obtain pleasant taste and acceptable fast disintegrating tablets, solvent evaporation technique with different types of taste masking polymers have been developed and described in literature as follows. Ofloxacin an antibiotic that imparts a bitter unpleasant taste inside the mouth, was reported to be microencapsulated with Eudragit E100 that is insoluble in mouth cavity pH, by application of solvent evaporation technique reported efficiency of microencapsulation was from 69 – 86 % [5]. Taste masked microspheres of diclofenac sodium was reported to be produced by solvent evaporation method and coated by shell of Eudragit EPO, later compressed in form of taste masked oro-dispersible tablets [21]. Another study conducted for the preparation of fast disintegrating oral tablets of promethazine HCL was microencapsulated by applying the solvent evaporation technique, and the outer shell for taste masking was amino alkyl methacrylate copolymer i.e. Eudragit E100. The drug polymer ratio used in this study was 1:1, 1:2, 1:3, 1:4 amongst which 1:4 ration showed entrapment efficiency of 85.41% with bitter taste
Moreover a study done by Sharma et al also reported fast disintegrating tablets of promethazine HCl, where taste masking of API was achieved by solid dispersion technique [23]. Another research reporting the microencapsulation of linezolid was done with help of solvent evaporation technique and were taste masked for production of FDTs [24]. Ondansetron hydrochloride was microencapsulated with help of polymer carrier system for production of rapid-disintegrating tablets by application of solvent evaporation technique. Ondansetron HCl’s complex with Eudragit EPO was first prepared by precipitation method, later the solution of ondansetron HCl and Eudragit EPO were prepared in ethanol with varying ratios of which (9.5:0.5 had 94.2% entrapment efficiency) and were injected in 0.1N sodium hydroxide solution with 500rpm stirring rate with help of a mechanical stirrer, to achieve microencapsulation [25]. Tinidazole fast disintegrating tablets were taste masked by microencapsulation of tinidazole in varying ratios with Eudragit E100 by using solvent evaporation technique, where 1:5 ratio of drug to polymer had an entrapment efficiency of 85% that were tasteless when applied in mouth cavity [26].

A number of techniques and tactics can be hybridized to solvent evaporation microencapsulation technique [27] that can make method even more feasible and easy, such as evaporation of solvent is initiated before the elimination of volatile solvent, that could be achieved by transformation of drug in a bigger volume of continuous where the leftover solvent can be removed by extraction [28]. This tactic can be used for preventing the formation of crystals at stage of evaporating solvent. A polymer can also be applied for the solvent extraction, and can thus decrease the stirring process and can be produced continuously [29]. Yoon Yeo et al reported a new method of microencapsulation and called it solvent exchange method that relies on the basis of principle that a layer of polymer is formed among the aqueous solution and water insoluble polymer at time of contact, in present study a dual microdispenser system was applied for microencapsulation. This new method was applied to overcome the limitations of previous methods such as delivery of bioactive agents for example proteins [30]. Another problem in solvent evaporation techniques is the monodispersity and uniform of the product, use of a microporous glass membrane can avoid this problem [31].

7. Conclusion

Microencapsulation is an efficient method for taste masking, different techniques can be applied for this purpose among which solvent evaporation is a reproducible, economic, that needs less effort and operating skills. Solvent evaporation technique has been successfully applied for taste masking of different drugs and especially in orodispersible tablets, to cover the unpleasant taste of drug. Fast disintegrating tablets taste masked with solvent evaporation technique produces less gritty particles that will produce a good feel in mouth. Use of hybridized tactics can make this technique more feasible and applicable to save time and money consumption. By application of microencapsulation technique such as solvent evaporation many bitter drugs can be produced as Fast disintegrating tablets that can be very useful for children and geriatric patients who have problem of dysphagia.

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