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Microencapsulation to Maintain the Activity and Stability of Drug Substances: A Review

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A B S T R A C T

Purpose: The microencapsulation method is one of the most widely used techniques to protect bioactive compounds from various environmental factors such as evaporation, oxidation, degradation of temperature, humidity, and light. Therefore, it can extend product shelf life and avoid damage so that it can last a long time and can still be utilized by the body well[1].

Selection of Data Sources: In compiling a review, this article used a literature study by finding sources or literature in the form of national and international journals in the last 10 years (2010-2020). Data search was also carried out using online media with the keywords as follows: microencapsulation, microcapsules, and microencapsulation methods. The search for the main references used in this review article was conducted through trusted websites such as Science Direct, Pubmed, Google Scholar, and other published and trustworthy journals.

Conclusion: Based on the results of several studies, it can be concluded that microencapsulation using several of the above methods can provide protection for the substance / drug against environmental influences, and it can maintain the stability of a substance / drug so that it can extend the drug release time.

Keywords: Activity, Stability, Coacervation, Microencapsulation, Spray Drying, Solvent Evaporation

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INTRODUCTION

The microencapsulation method is one of the most widely used techniques to protect bioactive compounds from various environmental factors such as evaporation, oxidation, degradation of temperature, humidity, and light. Therefore, it can extend product shelf life and avoid damage so that it can last a long time and can still be utilized by the body well[1].

There are several microencapsulation methods based on particle size such as freeze draying, spray draying, cooling, fluid bed coating, coacervation, and liposome entrapment. In the microencapsulation technique, the material used in the coating can be a polymer. Polymers have certain physicochemical properties so that they have different structures and characteristics. The polymer used must be able to provide a cohesive thin layer with the core material, must be chemically mixed, but must not react with the core (inert), and must have properties suitable for coating purposes[2]. In this review article, we will discuss about microencapsulation in general and its application to maintain the activity and stability of a substance or core material so that it can extend the release time of the drug.

Microcapsule

A microcapsule is a microscopic tube covered with a rigid and smooth wall resulting from the microencapsulation process[3]. Microcapsules measuring 1.0-5000 µm can be round, rectangular or irregular in shape[4].

Advantages of Microcapsules

With the polymer wall layer, the core substance will be protected from the influence of the outside environment. Microencapsulation can prevent discoloration and odor, and it can maintain the stability of the core substance which is maintained over a long period of time. It can be mixed with other components that interact with the core substance[3].

Disadvantages of Microcapsules

Incomplete or uneven coating of the core material by the polymer will affect the release of the core substance from the microcapsules, so microencapsulation technology is needed. The correct types of coating polymers and solvents that are suitable for the core material must be selected in order to obtain good microcapsule results[3].

Microencapsulation

Microencapsulation is a direct coating technique of active ingredients in the form of fine particles of solids, liquids and gaseous materials in small capsules that release the active substance in a controlled manner[5]. Microencapsulation is a process in which small particles or liquid droplets are wrapped or coated by polymeric material to produce small particles, which are called microcapsules or microspheres[2,6].

The purpose of the microencapsulation process is to increase the stability and solubility of a material, to control the release of active compounds, to produce solid particles coated with certain coatings and to minimize loss of the content of these materials[7].

The Advantages of Microencapsulation

The advantages of this technique are that it is able to regulate the core material (cover the unpleasant taste and smell of the core material), protect the core material (prevent changes and reduce the content of the core material), increase the stability of the core material during the production process to the final product (reduce evaporation of active ingredients, reaction with air, water and other materials, and the degradation process), and controlling the process of releasing the core material[8].

Microencapsulation Characterization

Microencapsulation is a technology to coat a core substance with a polymer wall layer, so that it becomes micro-sized small particles. With this polymer wall layer, the core substance will be protected from the influence of the outside environment. The core material can be solid, liquid or gas. Microcapsules are heterogeneous particles in which a membrane shell surrounds the nucleus to form a covering layer. Microcapsules are microscopic particles surrounded by a wall that can control the release of the core material[9]. Microcapsules measuring 1.0-5000 μm can be round, rectangular or irregular in shape[4].

The size of the microcapsules varies depending on the method and the particle size of the core material used. Factors that influence the success of the microencapsulation process include the physicochemical properties of the core or active substance, the coating material used, the microencapsulation process stage (single / stratified), the properties and structure of the microcapsule walls, and the manufacturing conditions (wet / dry)[10].

METHODS AND DATAS

In it compiling process, this review article used literature studies by finding sources or literature in the form of national and international journals in the last 10 years (2010-2020). Data search was also carried out using online media with the keywords as follows: microencapsulation, microcapsules, and microencapsulation methods. The search for the main reference used in the review article was conducted through trusted websites such as Science Direct, Pubmed, and Google Scholar, and other published journals.

RESULTS AND DISCUSSIONS

No.	Method	Title	Active Substances	Result	Author
1.	Spray Drying	Microencapsulation by coacervation and Ketoprofen Spray Drying Using Pregelatinized Cassava Starch Phthalates as coating excipients	Ketoprofen	Ketoprofen microcapsules made by spray drying method has a nearly spherical shape and have a smooth and concave surface. The microcapsules produced also had a lower index of expansion and drug release in the acid medium than the base medium so that the drug release could be tolerated and could be used as a slow release preparation.	11
		Isoniazid Microencapsulation Using *Sodium Carboxy methyl cellulose* (NaCMC) as a Polymer with Spray Drying Method.	Isoniazid	Characterization tests that have been carried out include assay and dissolution tests supported by particle size distribution analysis, SEM, XRD, DSC and FT-IR. The obtained results stated that the microcapsules formed meet the requirements of the microcapsules in general and have confirmed the results of the dissolution test, and the isoniazid microcapsules formed have a spherical shape.	12
2.	Solvent Evapora tion	Metronidazole Microencapsulation with HPMC Polymers Using Solvent Evaporation Method	Metronidazole	The metronidazole microcapsules produced by the solvent evaporation method have an almost perfectly round shape and slightly yellowish white in color. The dissolution profile shows that the release of metronidazole in the microcapsules is also slower.	13
		Microencapsulation of Atenolol with Albumin Using the Solvent Evaporation Method	Atenolol	The atenolol microcapsules produced have a spherical shape with a particle size of 212-2000μm. The dissolution results showed that the release of atenolol in the microcapsules would be slower.	14

		Pyrazinamide Microencapsulation Using Mannitol with Solvent Evaporation Emulsification Method	Pyrazinamide	The pyrazinamide microcapsules produced by this method have an almost spherical shape coated with mannitol. The dissolution of microcapsules can also be slowed down so that the active substances can be released slowly.	15
		Microencapsulation of Carbamazepine with HPMC Polymer Using Solvent Evaporation Emulsification Method The	Carbamazepine	The carbamazepine microcapsules prodced have a nearly perfectly round shape with a slightly yellowish white color. The dissolution profile shows that the release of carbamazepine in the microcapsules is slower the more the polymer is added.	16
		Microencapsulation of Paracetamol with Solvent Evaporation Method Using Sodium Carboxymethyl (NaCMC)	Paracetamol	The paracetamol microcapsules produced have an almost spherical shape covered by a coating. In the dissolution test, the release of paracetamol in the microcapsules was also slowed down due to the influence of the polymer.	17
3.	Phase Separation by Coacervation	Ketoprofen Microencapsulation Using Coacervation and Spray Drying Methods Using Pregelatinized Cassava Phthalate Starch as Excipient	Ketoprofen	The ketoprofen microcapsules made by the coacervation method have a non-spherical shape and have a rough and hollow surface. . The microcapsules produced also had a lower index of expansion and drug release in the acid medium than the base medium so that the drug release could be tolerated and could be used as a slow release preparation.	18
		Microencapsulation of Xylitol with Multiple Emulsions Followed by Complex Coacervation	Xylitol	The xylitol microcapsules produced are mostly spherical, with the core completely covered in wall material in all treatments. The xylitol microcapsules obtained by complex coacervation showed a mean size of between 78.45 and 109.31 µm, as would be expected for the coacervated microcapsules. Xylitol is very soluble in water.	19

Based on data obtained from literature search results, microencapsulation is a stable system due to a layer of material that provides physical protection and forms a barrier to the presence of oxygen and other small molecules[20]. Substances that are not resistant to environmental influences, such as proteins and enzymes, can be maintained by microencapsulating them. Microencapsulation techniques have been widely used to protect active substances from degradation processes due to the influence of light, heat, humidity and air by reducing contact with the environment[21]. The microencapsulation process can protect active substances from environmental influences or increase the stability of the preparation[22].

The spray drying method is a microencapsulation method that is commonly used to dry a liquid material through hot gases. In this method the microcapsules that are formed generally have an almost spherical shape with a smooth and concave surface[12].

In the Solvent Evaporation method, the working principle of this method is to dissolve or disperse the active substance into a polymer solution and then emulsify it into an external phase in the form of water or oil. The microcapsules will be formed and then continued with the solvent evaporation and polymer deposition process[23]. The coating used is dispersed in a volatile solvent, which is not mixed with the liquid carrier phase. In another container, the polymer coating solution is added to the core material and stirred with a homogenizer at a determined rate, afterward; the core coating which is dispersed in the liquid carrier phase is added gradually to obtain the appropriate microcapsule size. Stirring is carried out at room temperature until all the solvent has evaporated[17,13,15].

In the coacervation method, a number of polymers are dispersed in a suitable solvent to form a coating solution then add the core material to it while stirring until homogeneous. Microcapsules are generally carried out in three processes, namely continuous stirring, non-intermixed phases forming, the attaching of the core coating material and the hardening of the coating[18].

The microcapsules obtained were characterized including yield process, shape and morphology, absorption efficiency, particle size distribution, expansion index, functional group analysis and drug release profile[18].

CONCLUSION

Based on the results of several studies, it can be concluded that microencapsulation using several of the above methods can provide substance / drug protection against environmental influences and can maintain the stability of a substance / drug so that it can extend the release time of the drug.

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