

Optimization of PVA Concentration and Receiver Phase Volume in the Preparation of Rutin Microparticles

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Abstract

Microparticles are used as a drug delivery system that can overcome various shortcomings of the active substance. Rutin, as a compound that has limited solubility and stability, is very suitable for being formulated into a microparticle system. This study was conducted to describe the effect of PVA concentration in the manufacture of rutin microparticles and the volume of the receiving phase on entrapment efficiency. The manufacture of microparticles is carried out by the solvent evaporation method. From the experimental results, the increase in PVA concentration did not significantly affect the entrapment efficiency of rutin in microparticle preparations. However, the volume of the receiving phase used significantly affects the entrapment efficiency of rutin in the microparticles.

Keywords : microparticles, PVA, rutin, solvent evaporation method.

INTRODUCTION

Rutin is a popular dietary flavonoid that has gotten a lot of press due to its therapeutic actions, which include antibacterial, anti-inflammatory, anticancer, and antidiabetic activities, among others. In the United States, there are currently around 860 rutin-containing products on the market. Rutin's main drawback is its restricted bioavailability, which is mostly due to its low water solubility, poor stability, and limited membrane permeability [1].

Various efforts have been made to overcome deficiencies in routine. increase bioavailability to improve routine profiles as drug compounds. Among them are efforts to synthesize a more soluble chemical derivative of rutin to improve water solubility and formula dissolution. The synthesized rutin derivative is exceptional in that it has a higher solubility and, as a result, a higher oral bioavailability [2]. Rutin formulation in the form of a self-emulsifying drug delivery system (SEDDS) with *Physalis peruviana* calyces extract. These findings suggest that integrating a calyces extract from *P. peruviana* into SEDDS is a promising technique for increasing the rutin inside this extract's oral bioavailability and hypoglycemic efficacy [3]. Ultrasonication is used to create starch nanoparticles (SNPs) for rutin encapsulation. SNPs produced with ultrasonic have the potential to encapsulate polyphenols for enhanced bioavailability, according to simulated in vitro digestion [4].

Microparticles, which range in size from 1 to 1000 micrometers, are used as multiunit drug delivery systems with well-defined physiological and pharmacokinetic benefits in order to improve efficacy, tolerance, and patient compliance [5]. Rutin formulations in the form of microparticles are expected to improve the characteristics of rutin as well as increase their bioavailability.

This study aims to serve as a basis for optimizing rutin microparticle formulations using a solvent evaporating technique. Optimization is carried out, including the concentration of poly vinyl alcohol as a stability enhancing agent and the volume of aquabidest as a receiving liquid, to obtain optimal entrapment efficiency.

MATERIALS

Rutin Hydrate (Tokyo Chemical Industry), acrycoat s100 (Corel Pharma Chem), ethanol, dichloromethane (Merck), poly vinyl alcohol (PVA) (PT. Triman Pharmaceutical Industries), aquabidest (PT. Whidatra Bhakti) dan methanol (J.T Baker).

METHODS

Rutin Microparticles Preparation

To the tune of 50mg of rutin and 100 mg of acrycoat s100 are dissolved in the ethanol mixture and dichloromethane with a ratio of 1:1 to 20ml. PVA is dissolved in aquabidest as a receiving solution. Put rutin and acrycoat s100 solutions into the receiving solution. Stirrer uses a speed of 500rpm for 2 hours at room temperature. Filter the microparticles that are formed and rinse with aquabidest three times. Dry at room temperature for a total of 2x24 hours [6].

Optimization PVA Concentration

At this stage, PVA, which is used as an increase in stability in the formation of microparticles, uses a 0.5%, 1%, and 1.5% concentration of the volume of aquabidest used. The entrapment efficacy of active substances in the microparticle system as a parameter to obtain the most optimal PVA concentration.

Optimization of Receiver Phase Volume

The receiving solution used in this method is aquabidest. The volumes used in this experiment were 100 ml and 50 ml. The presence of aquabidest affects the microparticles formed. It will be interesting to see the effect of the volume of the receiving solution on the efficiency of entrapment of the formed microparticles.

Determination of Entrapment Efficiency

The entrapment efficiency of the rutin microparticle is carried out by first preparing the microparticles. 5mg of rutin microparticles was dissolved using 10 ml of methanol. Take 2.5 ml and dilute it with 5 ml. Measure the absorbance of the sample using Spectrophotometry UV at a maximum wavelength of 257 nm. Calculate the measured rutin

concentration and calculate the entrapment efficiency by comparing the measured rutin amount with the initial rutin level concentration entered.

RESULTS & DISCUSSION

This research is an experimental study to provide an overview of optimization in the manufacture of microparticles. Because of its potential benefits such as enhanced bioavailability, reduced risk of systemic toxicity, reduced risk of local irritation, and predictable gastric emptying, microparticulate drug delivery system has recently received a lot of attention in comparison to single unit systems [7]. Optimization of the factors in the manufacture of microparticles is very important in order to estimate the desired results.

Microparticles are made using a solvent evaporation technique which is quite effective and in accordance with the characteristics of the active substance and polymer used. Ethanol was used as a cosolvent to dissolve rutin. while the addition of dichloromethane will help the solvent evaporation process run faster to produce microparticles. In compared to ethanol, microparticles made with dichloromethane as the organic solvent had better sphericity, a more regular form, and a smooth surface, making dichloromethane a more ideal organic solvent for this purpose [8].

PVA is an effective polymer as a stabilizer of the receiving phase in the manufacture of microparticles. The results of the optimization of PVA levels showed that the use of 0.5% PVA resulted in a percent entrapment efficiency (%EE) of 27.72 ± 5.9 . PVA 1% yields a %EE of 27 ± 5.52 , while PVA 1.5% yields a %EE of 30.59 ± 4.07 . This indicates that the increase in PVA levels did not significantly increase the %EE rutin in the microparticle system. This is different from the results of research conducted by Mawazi and friends, where increasing levels of PVA can prevent the formation of new crystals of carbamazepine [9]. However, these results are in line with the results of research on the effect of PVA on the manufacture of ibuprofen microparticles as a sustained release preparation [8].

The use of aquabidest as the receiving phase in the manufacture of microparticles will greatly affect the % EE of the active substance used. This is strongly influenced by the solubility of the active substance in the receiving phase. Rutin is a compound that is slightly soluble in water. The results of this study indicate that the use of water volume significantly affects the %EE rutin in the preparation of microparticles. At 100 ml of aquabidest volume, the %EE is 26.83 ± 2.85 , and at 50 ml of aquabidest volume it becomes 55.04 ± 1.65 . By reducing the volume of aquabidest, the solubility of rutin as the receiving phase will also decrease so that the entrapment rutin becomes larger. This result is different from Pavelková & Vysloužil study, which showed that increasing the volume of the receiving phase had a positive impact on the production of ibuprofen microspheres. This is because it is influenced by the solubility of the active substance in the receiving phase and the method of making microspheres used [10].

CONCLUSION

In the manufacture of rutin microparticles using the solvent evaporation method, various optimizations are needed to produce good microparticles. The entrapment efficiency parameter becomes very important in determining the success of a method and material used as microparticles. The use of PVA as a stability enhancer is needed to produce good microparticles. This study showed that the increase in PVA did not significantly affect the amount of rutin incorporated into the microparticles. However, this is not the case with the aquabidest volume as the receiving phase. Reducing the volume of the receiving phase significantly increased the %EE of ibuprofen in the microparticle preparation.

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