Original Article

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Utilization of Eggshell Powder as Excipient in Fast and Sustained Release Acetaminophen Tablets

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Abstract

Eggshell powder has been investigated for the new application as pharmaceutical excipient in tablet dosage form. Acetaminophen was used as a model drug in this study. Four different eggshell powders were prepared. These included untreated eggshell powder, water treated, ethanol treated and chloroform treated eggshell powders. The treated samples were prepared by surface modification using 1.0 % w/v stearic acid in solvent namely deionized water, 95 % ethanol and chloroform. The tablets containing acetaminophen, eggshell powder and microcrystalline cellulose were prepared by direct compression method. Dissolution studies of four acetaminophen formulations in pH 5.8 phosphate buffer were performed using USP Dissolution Apparatus II. The results show that immediate release of acetaminophen was obtained from tablets containing untreated eggshell powder whereas sustained release of the drug was obtained from the tablet formulations containing three different treated eggshell powders. Sustained release of the drug may be due to hydrophobic nature of the treated eggshell powders. It was also found that the degree of hydrophobicity of the treated eggshell powders depends on the type of solvent used in surface modification process. The results obtained from this study show that eggshell powder appears to be applicable as a pharmaceutical excipient to control the drug release from the tablet. Additionally, this finding may be useful to generate public interest in development of biomaterials from eggshell waste by proposing the new application of eggshell powder in pharmaceutical industry.

Keyword: Eggshell, Drug release, Acetaminophen, Excipient, Bioresource utilization

INTRODUCTION

Hen eggshell, a waste material from domestic sources such as hatcheries, poultry farms, egg product factories, homes and restaurant, has been a serious matter as global awareness regarding organic waste materials and pollution problems was increased[1]. The egg-breaking industry spent up to $ 100,000 a year to dispose of eggshells in landfills, many of which are reaching capacity. Additionally, landfills do not want eggshells because the protein-rich membrane which adheres to the shell attracts rats and other[2]. In 1997, the same industry consumed about 50 million cases of egg, producing more than 120,000 tons of unprocessed eggshell waste with disposals costs between $ 25,000 and $ 100,000 per year[3]. In Taiwan, for example, the annual generation of eggshell waste from the food processors was estimated to be over 1.3 x 104 ton on the basis of 7.1 x 109 of pieces of hen eggs[4]. Most eggshell waste is discarded without further processing by sending to landfill at a cost more than $ 40 a ton depending on the location of the landfill[2].

It is necessary to find an alternative method which would transform the waste eggshells into a valuable item; giving financial benefits to the competitive egg processing industry. Apart from giving manufacturers a new profit stream, it would help overcome the high disposal costs and environmental concerns[3,5]. The waste eggshells are sometimes spread on land as a fertilizer source. Many

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studies have looked for ways to utilize the eggshell waste by, for example, using eggshell powder as a stabilizing material for improving soil properties[6], as coating pigments for ink-jet printing paper[7], as food additive[8] and as a source of calcium in animal and human nutrition[1,9-11].

The chemical compositions (by weight) of by product eggshell are as follows: calcium carbonate (94%), magnesium carbonate (1%), calcium phosphate (1%) and organic matter (4%)[4]. As the major component of the eggshell is calcium carbonate, it may be used to replace calcium carbonate, which is used as pharmaceutical excipient, in solid dosage forms. In addition, calcium carbonate from eggshell has an advantage for not containing toxic elements like calcium carbonate from oyster shells which contains lead vestige among the others potential toxical elements such as aluminum, cadmium and mercury[12]. We have performed a study on preparation and characterization of eggshell powder. The results of our work show that eggshell powder has appropriate physical properties for use as an excipient in solid dosage form[13]. Therefore further study on application of the eggshell powder in tablet formulation has been carried out. The main objective of this study was to develop the eggshell powder for use as a pharmaceutical excipient in tablet dosage form. It is hoped that this alternative application of eggshell would help overcome global eggshell waste problem.

MATERIALS AND METHODS

Eggshell particles preparation

The hen eggshell was collected from the canteen of Faculty of Pharmacy, Mahidol University. The eggshell membrane was removed and the eggshell was washed thoroughly with tap water. Then the eggshell was boiled in deionized water for 30 minutes. It was dried in hot air oven at 80˚C for 2 h. The dried eggshell was crushed and ground using porcelain mortar and pestle. The eggshell powder which passed 200 mesh sieve was used in the study.

Treated eggshell particles preparation

Stearic acid was obtained from Unilab, Australia, chloroform was obtained from Labscan, Bangkok, Thailand, ethanol was obtained from Merck, Darmstadt, Germany. Acetaminophen was obtained from Usine de Roussillon, France. The water used was deionized water.

20 g of the eggshell particles was treated with 20 mL of 1.0 % w/v stearic acid solution in three different solvents, i.e., water, 95% ethanol or chloroform in glass mortar. In case of water, boiling water was used and the sample was dried in an oven at 45 ˚C overnight. In cases of ethanol and chloroform, the experiments were carried out at room temperature and the samples were left overnight at room temperature.

Preparation of acetaminophen tablets

Acetaminophen tablet was prepared by mixing the dry powder of acetaminophen, eggshell powder and microcrystalline cellulose (Avicel PH 102). 660 mg of the mixture containing 60 mg acctaminophen, 240 mg eggshell powder and 360 mg microcrystalline cellulose (Avicel PH 102) was compressed at a compaction pressure of 1 ton in a hydraulic press (Enerpac). The punches used were flat face with a diameter of 13 mm. The selected compaction pressure was maintained for 10 s to allow the development of most possible plastic deformation on the powders, to avoid the effect of different dwell times producing different degrees of plastic deformation and their consequent effect on the tablet physical properties.

Dissolution studies

In vitro drug release of formulated eggshell powder tablets was determined

using USP Dissolution Apparatus II (Paddle type). The dissolution test was performed using 900 mL pH 5.8 phosphate buffer at 37±0.5°C. The speed of rotation of paddle was set at 50 rpm. 5 mL samples were withdrawn at 5, 10, 15, 20, 25, 30 minutes, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10 hours and absorbance of the solution was measured by using UV spectrophotometer (U-3000 spectrophotometer, Hitachi, Tokyo, Japan) at a wavelength of 243 nm. The amount of drug release was determined from the standard curve. Mean and standard deviation of 6 tablet samples were calculated. The study was performed using freshly prepared tablets and the tablets stored at controlled temperature (45ºC) for one month.

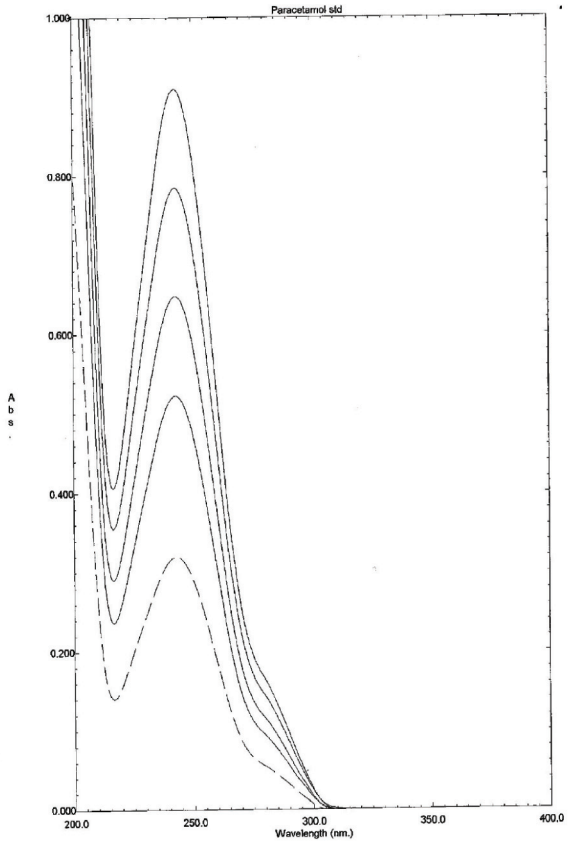

Figure 1. Wavelength scan of different concentrations of acetaminophen in pH 5.8 phosphate buffer solution

RESULTS AND DISCUSSION

In this present study, acetaminophen was used as a model drug. Figure 1 shows acetaminophen wavelength scan with λ_{max} of 243 nm. Figure 2 represents the standard curve of acetaminophen. The dissolution profiles over 10 hours period of all four formulations were shown in Figures 3 and 4. From Figure 3, it was found that, at 20 min, the total percent release of acetaminophen from freshly prepared untreated eggshell powder tablets, water treated, ethanol treated and chloroform treated eggshell powder tablets were 100.00±2.50%, 33.40±2.03%, 18.26±1.01% and 14.35±0.27% respectively. At 10 hours, the percent drug release from water treated, ethanol treated and chloroform treated eggshell powder tablets were increased

to 90.53±3.71%, 55.93±4.15% and 57.78± 4.12 %, respectively. For untreated eggshell powder tablets, fast release of the drug was obtained. This indicates that untreated eggshell powder behaves in the same way as synthetic calcium carbonate which is used as a buffering and dissolution aid in dispersible tablets[14].

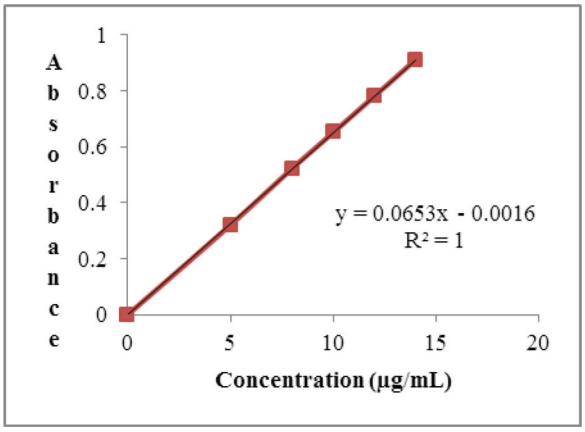

Figure 2. Calibration curve of acetaminophen in phosphate buffer pH 5.8

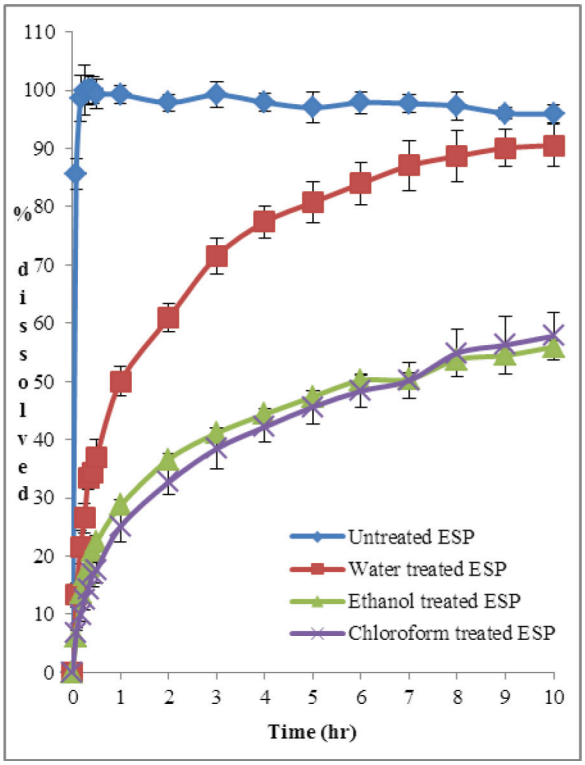

Figure 3. In vitro release of acetaminophen from freshly prepared tablets

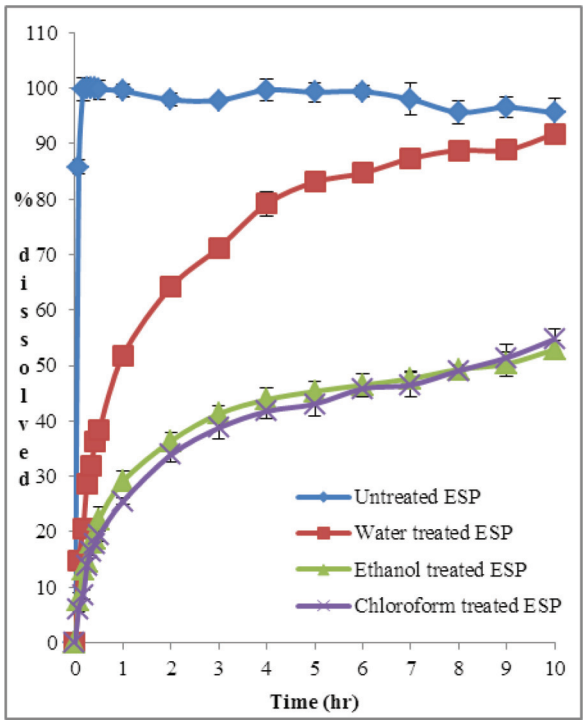

Figure 4. *In vitro* release of acetaminophen from tablets after one month storage at 45°C

The dissolution profile of water treated powder tablets shows similar pattern when compared to those of ethanol and chloroform except for that the extent or percent drug release from water sample was higher than those of the other two samples. In addition, the results obtained after storage for one month at 45°C were presented in Figure 4. The results indicated that, for all formulations, there was no change in drug release pattern after storage for one month at 45°C. This may indicate the good stability of the formulations.

Figure 5 shows the mechanism of four formulations in dissolution medium. Being powder coating and not a typical film causes the drug dissolution extension. The possible reason for release extension is the hydrophobic nature of stearic acid, which retards or prevents penetration of dissolution medium into tablet core. However, due to the effect of stirring given to the dissolution medium, some erosion of the coating layer or pore formation on coating layer may occur. This leads to a limited entry of dissolution medium into the core. The untreated tablets swell and disintegrated into fine particles within a few minutes after being in contact with pH 5.8 phosphate buffer solution. This results in immediate release of the drug. On the other hand, the treated tablets surface is hydrophobic in nature. According to Figure 5, the chains of stearic acid dissociated in the acid medium and calcium stearate formed on the surface of the particle. This prevents or retards wetting of the tablet surface which in turn results in the delay release of the drug.

Among the three treated formulations, the rate and extent of the drug release from the water treated eggshell powder was higher than that of the two treated samples. This may be due to impaired release retardation of the coat formed by using water. Ethanol and chloroform treated samples show good retardation of the drug release. These two treated samples could retard and prolong the release up to 10 h or longer.

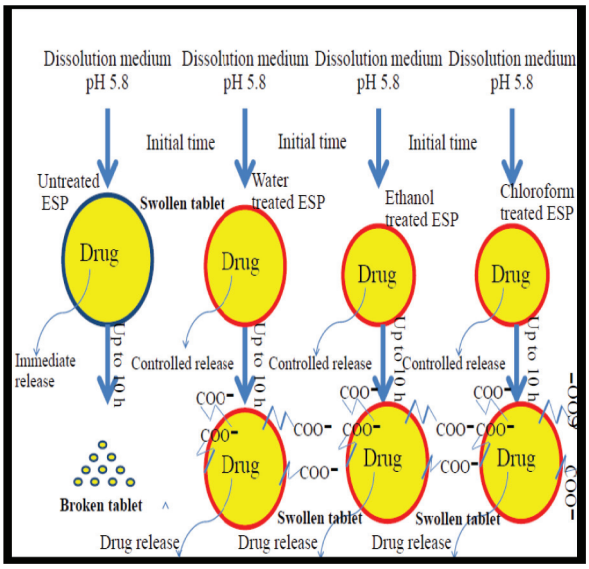

Figure 5. Diagrammatic representation of drug release from untreated and treated eggshell powder formulations in pH 5.8 phosphate buffer

CONCLUSION

Based on the results of this study, it can be concluded that eggshell powder could be used as tablet excipient. It can be employed as diluent and/or drug release controlling agent in the tablet formulation. The untreated eggshell powder was suitable for the fast release formulation while the treated eggshell powders were suitable for the controlled or sustained release formulation. Among three of the treated formulations, water treated method was found to be the best method regarding economical and environmental concerns.

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