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Effect of Sonication on Improving Curcumin Encapsulation Quality: Preparation and Characterization

Aji Prasetyaningrum, Aulia D. Ashianti, Nur Rokhati, Mohamad Djaeni, and Bakti Jos

Department of Chemical Engineering, Faculty of Engineering, Diponegoro University, Semarang 50275, Indonesia

Abstract

This study investigates the enhancement of curcumin encapsulation through ultrasound-assisted techniques, addressing its inherent challenges of low aqueous solubility and instability. Curcumin, a polyphenolic compound with significant health benefits, was encapsulated using a combination of alginate and chitosan biopolymers. The encapsulation process employed ultrasonication to improve efficiency and material properties. Optimum encapsulation efficiency (89.86%) and swelling ratio (1.78 g/g) were achieved at 9 minutes of sonication. The results were characterized using Scanning Electron Microscopy (SEM), which revealed surface cracks on the encapsulated particles caused by ultrasound-induced cavitation. Ultrasound treatment enhanced the interaction between core and shell materials, reducing particle size and increasing stability. However, excessive sonication led to adverse effects such as droplet recoalescence and structural degradation. The swelling ratio initially increased with sonication time but declined after reaching an optimal duration, reflecting changes in intermolecular interactions and hydrophilicity due to cavitation effects. This study highlights ultrasound as a promising method for optimizing curcumin encapsulation by enhancing bioavailability and environmental stability. The combination of ultrasound with ionic gelation offers a scalable approach to developing functional food and pharmaceutical products. Future research should explore optimized ultrasound parameters and alternative biopolymers to further improve encapsulation outcomes. These findings pave the way for innovative applications in nutraceuticals and drug delivery systems, emphasizing the potential of ultrasound technology in addressing the limitations of bioactive compound delivery.

Keywords: Curcumin; Ultrasonication; Encapsulation; Alginate; Chitosan

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1. Introduction

Curcumin is an active compound found in turmeric (Curcuma longa), which gives it a bright yellow color. Curcumin is also known as diferuloylmethane and has the chemical formula $C_{21}H_{20}O_6$. Curcumin belongs to polyphenol group that has two tautomeric forms, namely ketone and enol, with ketone form being more dominant in solid state. This compound has many benefits such as antioxidant, anti-inflammatory and anticancer [1]. However, curcumin has major challenges in its application, namely low solubility in water and limited bioavailability. To overcome these limitations, encapsulation method has developed as an effective solution to increase its stability and bioavailability [2]. Encapsulation is process of entrapping active compounds into a carrier material. Encapsulation aims to protect curcumin from environmental degradation, increase its stability and solubility, and slow its release in the body. Encapsulation not only protects, improves shelf-life and bioavailability, overcomes the solubility barrier, and controls release of delicate chemicals but also enables administration of lesser amounts of these compounds, reducing likelihood of side effects and possible syndromes [3].

This process involves the use of coating materials to improve product stability and facilitate handling of active ingredients such as bioactive compounds [4]. Alginate and chitosan are two biopolymers that are often used in encapsulation because they have good compatibility and form polyelectrolyte complexes through ionic gelation that can improved capsule stability. Alginate which is hydrophilic and chitosan which is biocompatible and easily degraded in the body are an effective combination to improve the stability and efficacy of encapsulation [5-6]. In the recent years, various delivery systems have been employed to protect curcumin using different wall materials and physiochemical and mechanical procedures, including encapsulation using emulsification, coacervation, solid lipid particles, nanostructured lipid carriers, spray drying, lyophilization and ionic gelation [7]. Ionic gelation method possible to encapsulate almost all components such as hydrophilic or hydrophobic, heat sensitive, fluid or viscous, solid or liquid

ones. Ionic gelation method allows bioactive compounds to be bound in polymer matrix through reaction between Ca^{2+} ions from calcium chloride ($CaCl_2$) with ionic groups from alginate, which forms a strong gel structure [8]. Ionic gelation is also widely used because it has many advantages such as cheap, simple and feasible process requiring no organic solvent and high temperature treatments [9].

The encapsulation of food ingredients into alginate matrices could be done following ionotropic gelation, a simple and effective process that does not require high energy, organic solvents and/or complicated technologies. Furthermore, core-shell materials synthesized using the ionic gelation method are reported to have low stability, larger, and non-homogeneous droplet sizes [10]. Ultrasound technology has proven effective in creating core-shell structures with certain physical and functional properties [11]. Ultrasound works by producing high-frequency sound waves that create cavitation phenomena in solution, which can help disperse active ingredients more homogeneously in polymer matrix, accelerate the absorption rate of wall material, and increase the interaction between active ingredients and wall material [12]. The feasibility of using ultrasound to encapsulate bioactive compounds is based on ability of this technology to reduce the size of emulsion droplets to a range smaller than 1 μm [13]. With combination of ultrasound technology and ionic gelation method, it expected to increase encapsulation efficiency, stability, and bioavailability of curcumin.

2. Materials and methods

2.1. Materials

Curcumin extract was obtained from SIGMA-Aldrich, alginate (molar mass 216.12 g/mol with CAS Number 9005-38-3 SIGMA-Aldrich, USA), chitosan (75-85% degree of deacetylation with CAS Number 9012-76-4 SIGMA Aldrich, USA), soybean oil, acetic acid, tween 80, calcium chloride, and aquadest.

2.2. Encapsulation of Curcumin

Encapsulation process comprised a two-step particle preparation methodology. Initially, 2% sodium alginate solution prepared in distilled water, stirred at 500 rpm for 45 minutes at ± 30°C. Concurrently, a curcumin solution was generated by emulsifying 1% curcumin extract in soybean oil to achieve homogeneity. Subsequently, Tween 80 and curcumin oil incorporated into alginate solution. This mixture then homogenized for 20 mins. Following this, solution subjected to sonication via ultrasound at varying durations (6-12 minutes). In second step, a 1% chitosan solution was formulated in acetic acid at pH 5, stirred at 500 rpm for 45 minutes at approximately ± 30°C. This chitosan solution subsequently combined with first step solution at a 1:1 volume ratio. Resultant mixture homogenized for 15 mins to attain uniformity. This uniform solution then injected into a 0.2 M $CaCl_2$ solution under continuous stirring. Formed particles allowed to stabilize in cross-linking solution for 30 minutes. Finally, they isolated by filtration and dried at ambient temperature for 48 hours.

2.3. Characterization

2.3.1. Encapsulation Efficiency

The encapsulation efficiency was assessed by quantifying the quantity of bioactive substance that remained unconfined within the alginate-chitosan beads subsequent to their immersion in a $CaCl_2$ solution. In this instance, the encapsulation efficiency denotes:

$$EE\ (\%) = (Qt - Qr)/Qt \times 100 \qquad (1)$$

Where Qt is the quantity of bioactive curcumin and Qr is the bioactive curcumin present in $CaCl_2$ solution after encapsulation.

2.3.2. Swelling Analysis

The assessment of swelling was conducted in a pH 7 buffer solution. The swelling percentage can be computed utilizing the formula:

$$Swelling\ ratio\ = (Ws - Wd)/Wd \qquad (2)$$

Ws represents the weight of the bead when wet, and Wd denotes the weight of the bead when dry.

2.3.3. SEM Analysis

The surface structure of the curcumin-encapsulated material was investigated using a SEM JEOL JSM-6510LA instrument. Before conducting analysis, samples underwent a process of gold metallization utilizing a sputter coating unit. During examination, the SEM was set to a magnification of 1.500× to observe the surface morphology of samples.

3. Results and discussion

3.1. Effect of Sonication Time on Encapsulation Efficiency

Encapsulation efficiency determines the levels of bioactive compounds in curcumin entrapped in alginate-chitosan beads. Effects of sonication time on encapsulation efficiency are shown in Figure 1. The results showed that optimum encapsulation efficiency and swelling ratio was obtained at the 9 min sonication. Ren et al. [14] stated that ultrasonication can significantly improve encapsulation efficiency with increasing sonication time. Acoustic cavitation generated by ultrasonic waves can alter macromolecular structures and enhance macromolecular interactions. The mechanical effect of acoustic cavitation can also increase mass transfer rate, contact frequency, and collisions between the shell and core, thus enhancing encapsulation efficiency [15]. Although increasing sonication time can enhance encapsulation efficiency, research by Huang et al. [16] suggests that an increase in sonication time may lead to a decrease in encapsulation efficiency. The ultrasonic cavitation effect may increase the probability of droplet rupture and delamination of the core-shell structure of composite particles, resulting in more loaded drug leakage and reducing encapsulation efficiency. A similar phenomenon also occurred in previous research by Prasetyaningrum et al. [17] where excessive ultrasonication reduced the encapsulation efficiency of citronella oil.

3.2. Effect of Sonication Time on Swelling Ratio

The effects of sonication time to the swelling ratio were evaluated at the range time of 0 min to 15 (Fig. 2). In the time range of 0 to 9 minutes, the swelling ratio increases from 0.74 g/g to 1.78 g/g. Ultrasonication for 9 minutes produces the highest swelling ratio of 1.78 g/g. However, in the time range of 12 to 15 minutes, there is a decrease in swelling ratio from 1.71 g/g to 1.47 g/g. With the addition of ultrasound duration, swelling ratio initially shows an increasing tendency and then a decrease. The increase in ultrasound duration enhances thermal effect of ultrasound waves, promoting intermolecular

motion and exposing hydrophilic groups, thereby increasing swelling ratio up to a certain limit [18]. However, excessive processing of ultrasound can result in merging of previously formed droplets, known as recoalescence. This phenomenon diminishes efficacy of encapsulation and leads to an enlargement of droplet size, thereby reducing particles' ability to swell effectively [10]. The swelling ratio typically rises as particle size decreases [18].

3.3. SEM Analysis

Surface morphology of alginate/chitosan/curcumin granules with the optimum variables at 9 minutes observed using Scanning Electron Microscope (SEM) analysis as shown in Figure 3. Surface morphology of curcumin granules have a rough surface structure without cracking in sample with ultrasound treatment, while samples without ultrasound treatment had rough and cracking surface morphology.

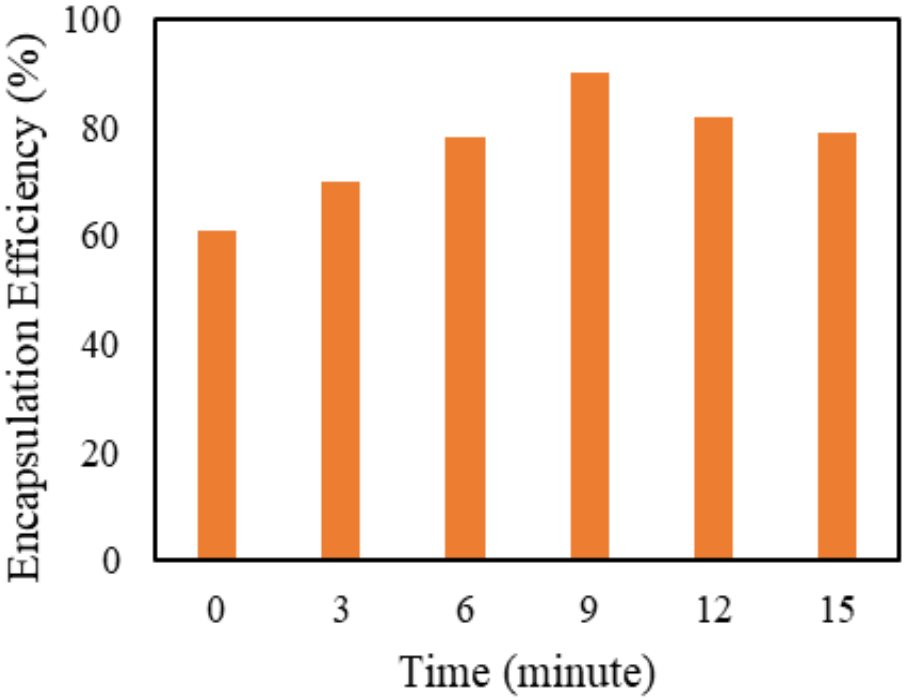

Figure 1. Effect of Sonication Time on Encapsulation Efficiency

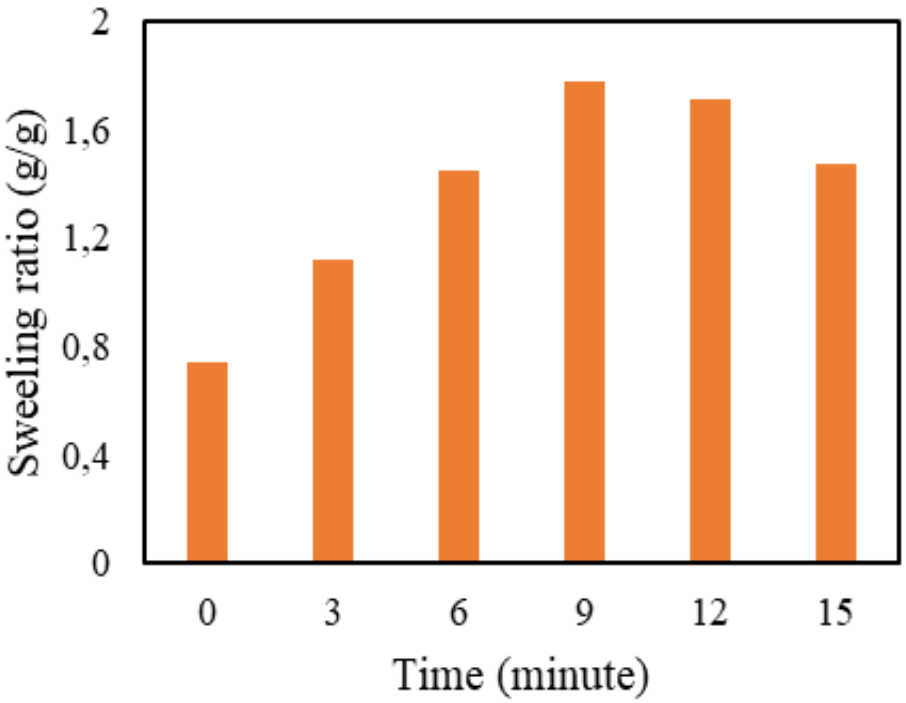

Figure 2. Effect of sonication time on swelling ratio

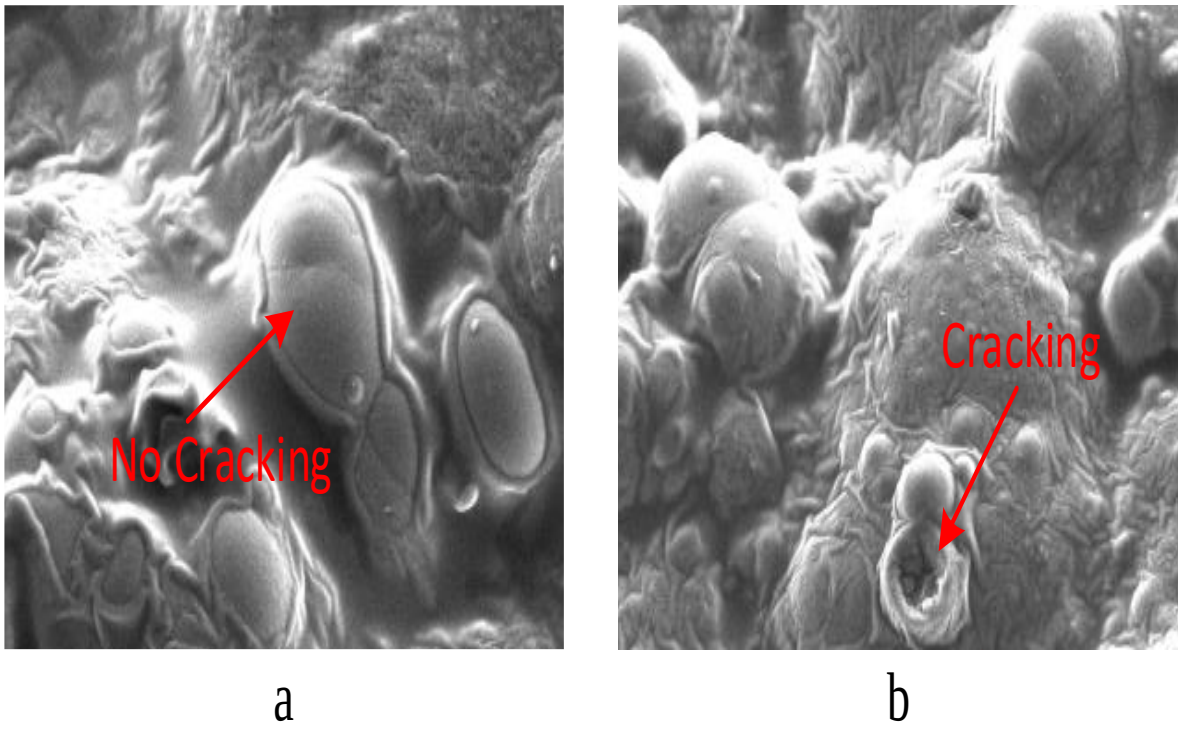

Figure 3. Morphology of (a) alginate/chitosan/curcumin (non-ultrasound); (b) alginate/chitosan/curcumin (ultra-sound)

SEM results reveal alterations on surface of sample beads subjected to ultrasound treatment. Changes observed on bead surface may be attributed to cavitation phenomenon, generating elevated stresses and shear forces. This leads to mechanical degradation of amorphous layer in wall material, ultimately reducing particle size and resulting in numerous cracks on bead surface. This phenomenon causes the disruption of glycosidic bonds and degradation of the carboxyl groups in alginate, causing the particle structure to become more relaxed, providing a larger space for the surrounding medium to penetrate the particles [19]. Similar instances of cracks were documented by Zhu et al., [20] where ultrasound-treated samples experienced damage due to ultrasound cavitation. Ultrasonic treatment causes the rupture and mechanical damage of beads through the collapse of cavitation bubbles, inducing high pressure gradients and high local velocities of liquid layers in their vicinity, resulting in shear forces capable of damaging beads [21].

4. Conclusion

It was suspected that time and power of sonication can influence the encapsulation efficiency. The mechanical effects resulting from the shear force due to bubble explosion can increase the contact frequency between the core and shell, which increases encapsulation efficiency. Increased swelling ability can be achieved with extended time and ultrasound power. Chemical and physical damage to the beads can be induced by facilitating water penetration, leading to an increased amount of absorbed water in the beads. Additionally, the SEM results indicate the presence of cracks attributed to the influence of ultrasound cavitation. This encapsulation of the curcumin can be a potential drug delivery system. This study highlights the considerable potential of ultrasound treatment in effectively regulating the release behavior of bioactive compounds from the encapsulation.

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