

INDONESIAN HALAL HARD CAPSULE

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Abstract

*Halal hard capsule have been made from Indonesian local plant, i.e. porang, *Amorphophallus oncophyllus*. The main component from porang, i.e. glucomannan, was extracted by maceration method using ethanol. A 4% of glucomannan was dissolved in demineralized water under heating condition to form a gel. Furthermore, the gel was molded to form a hard capsule. For improving the hard-capsule quality, the addition of papaya leaves and pineapple fruit extracts were investigated. The effect of temperature and time of hard capsule formation were also observed. The best condition obtained at 40°C for 30 minutes. The appearance of porang hard capsules with and without papaya leaves and pineapple fruit extracts were similar with commercial hard capsule. The solubility of porang hard capsule in water and acid solution are around 15 and 5 minutes, respectively. The result also has no significant difference from commercial hard capsules that available in the market.*

Keywords: Porang; glucomannan; extract; capsule; Indonesia.

INTRODUCTION

Indonesia is a second nation with biodiversity in the world. Several scientists were used Indonesian plant extract as anti-oxidant (Indis and Kurniawan, 2016), corrosion inhibitor (Firdausi and Kurniawan, 2016), water repellent (Kurniawan et al., 2017), and membrane (Kurniawan et al., 2014). One of the original plants from Indonesia that can be developed is Porang (*Amorphophallus oncophyllus*). Porang is the source of a water soluble fiber and has been consumed and used as traditional medicine in China and Japan (Chen et al., 2014, 2016; Xiao et al., 2015). This plant is a tub-shaped plant that have the primary component as known glucomannan. Glucomannan is a high molecular polysaccharide (Chen et al., 2016). The

structure of glucomannan as residues of mannose and glucose, link together by β -1.4 in a molar ratio of 1.6:1.0 with a low degree of acetyl group sat the C-6 position. Glucomannan is considered as an indigestible dietary fiber being resistant to hydrolysis by the action of digestive enzymes in the human gut (Chen et al., 2014; Zhou et al., 2014; Li et al., 2015). The FDA (Food and Drug Administration, USA) was stated that glucomannan is safe biomaterial and drawn much attention for being used in target delivery systems for controlled release of drugs. So, it is possible to use glucomannan as the material of hard capsule because it is able to coagulate into gel, fiber content, and high-water holding capacity. However, glucomannan has a high molecular weight (500-2000kDa) and the maximum

solubility in water is 1%, yielding a solution of high viscosity (Chen et al., 2016; Rabadiya, 2013). These properties are not favorable for preparing hard capsule. By means of oxidation, the chemical structure of glucomannan can be optimized to increase solubility and hydrophobicity, making it more suitable for hard capsule material (Chen et al., 2014, 2016; Li et al., 2015; Zhou et al., 2014).

Hard capsules are one of the most important needs in the pharmaceutical field (Chen et al., 2016; Gullapalli and Mazzitelli, 2017; Hoag, 2017; Rabadiya, 2013). Gelatin hard capsule are the most common form of capsules which has many advantages as pharmaceutical excipient, such as better bioavailability than tablet, faster rate of drug release, simpler manufacturing process, easily filled with combination form of drug, masks tastes and odor (Hoag, 2017; Rabadiya, 2013; Rana et al., 2011). The main raw material used in the manufacture hard capsules are gelatin. The main characteristic of gelatin which made it special is its ability to form gel reversibly by hydrogen bonding at low temperature. Gel of gelatin can dissolve at temperature above 35°C, so gelatin capsule will dissolved in the body's biological fluids (37°C). Gelatin is animal-derived material. It could be obtained from bovine or porcine tissues (Berardi et al., 2017; Duconseille et al., 2015; Gullapalli and Mazzitelli, 2017; Hoag, 2017; Rabadiya, 2013; Sherry Ku et al., 2010). The animal source of gelatin, especially porcine-derived material could be a problem for certain consumers such as for Moslem because in Islam, everybody forbid to use

and consume it (Abdullah Amqizal et al., 2017; Ahmad et al., 2017; Riaz and Chaudry, 2003; Tieman and Ghazali, 2014). Therefore, there is an urgent demand on developing plant-derived material to produce hard capsule.

In this study, we fabricate halal hard capsule by glucomannan obtained from porang. The effect of papaya leaves and pineapple fruit extracts in production process were also investigated. The use of natural ingredients from plants and the production process without haram addition cause porang hard capsule tend to halal.

METHODOLOGY

Materials

Ethanol and demineralized water were purchased from chemical local shop and used without any purification. A 3 year old of porang were cultivated and brought from Segulung Village, Madiun, and East Java, Indonesia. Porang were peeled, washed and cut into small pieces, and then dried at room temperature. The dried porang were mashed into a flour. The porang flour was purified by 50% ethanol, and then diluted until 100 mL. This mixture was stirred for 30 minutes. After 30 minutes, the mixture was filtered and dried to remove solvent. This procedure was repeated three times to get a pure glucomannan. Glucomannan from porang was characterized by Fourier transform infrared (FTIR, Shimadzu-8400S) using KBr-disk technique.

Fresh papaya leaves were collected from garden at Institut Teknologi Sepuluh Nopember, Surabaya, Indonesia. The collected leaves were cleaned, cut into a small pieces and dried. The dried leaves

was mashed into a powder. The leaves powder was extracted by maceration method using 96% ethanol. Furthermore, the extract was filtered and concentrated by rotary evaporator.

Pineapples fruits were bought in local market. The fruits were peeled and taken the cores. The cores was sliced and blended with an equal weight of demineralized water. Furthermore, it was filtered to remove fibrous material and then centrifuged for 30 minutes. This process obtaine pineapples fruit extracts.

Methods

Various weight (1-4 g) of glucomannan from Porang were dissolved in 100 mL distilled water by stirring at room temperature until form a gel. The aim of this work is to know the best formulation for fabrication of hard capsule. Furthermore, Pairs of molds were dipped into the gel solution to form porang hard capsule. The effect of pineapple fruit and papaya leaves extracts in the porang hard capsule was investigated. The addition of those extract is to improve the physical properties of porang hard capsule.

The extract of papaya leaves or pineapple fruit was added to the gel solution of porang under various stirring condition (10-50 minutes). The gel solution of porang in the present of papaya leaves or pineapple fruit extract was heated at various temperature, i.e. 30°C (room temperature), 40°C and 50°C. Afterward, the gel solution with pineapple fruit or papaya leaves extract was formed into hard capsule by molding and dried. The dried hard capsule was stripped from the mold.

Characterization of halal hard capsule from porang was observed by viscosity value and solubility properties. Viscosity of porang gel solution with and without papaya leaves or pineapple fruit extract was measured according to ASTM D-1200-94 by viscometer ford cup.

The porang hard capsules with and without papaya leaves or pineapple fruit extract were tested for solubility in water and acid solution. All porang hard capsules were filled with certain drugs and then dissolved in the test solution (i.e. water and acid solution). The release time of the drug was observed and recorded. The result will be compared with the drug release time from commercial gelatin hard capsule.

RESULTS AND DISCUSSION

Characterization of Glucomannan

The porang flour and lucomannan from porang was characterized using FTIR. The result can be found in Figure 1. We found that glucomannan has several functional groups, including hydroxyl group of polysaccharide which shown by strong vibration at 3422 cm^{-1} , methyl group at 2928 cm^{-1} , and acetyl group at 1746 cm^{-1} . Those functional groups is characteristic of natural glucomannan (Jian et al., 2015; Zhang et al., 2001).

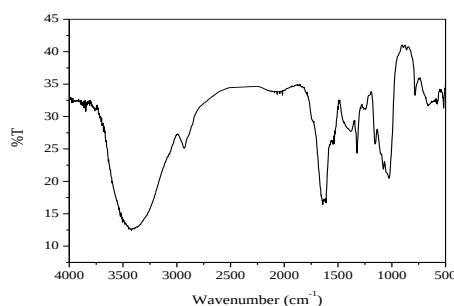


Figure 1. FTIR spectra of glucomannan from porang.

Indonesian Halal Hard Capsule

Halal hard capsule was successfully fabricated from Porang (*Amorphophallus oncophyllus*). The obtained hard capsule is called “halal” because we only use plant-derived material. The addition of pineapple fruit and papaya leaves extract in the hard-capsule process also shows the significant effect. Those extract were proved can be improve the properties of porang hard capsule (Figure 2).

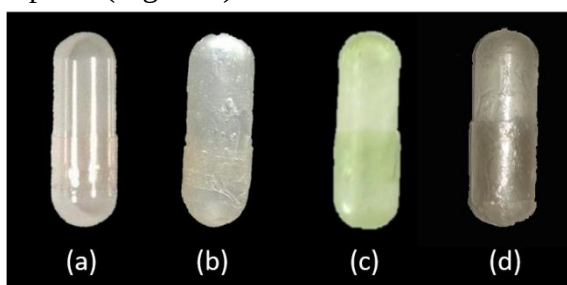


Figure 2. Hard capsule from gelatin (a), porang without extract addition, porang with papaya leaves extract (c) and porang with pineapple fruit extract (d).

Figure 2b shows that porang have a good result to be hard capsule. According to Xu et al (2007), gel solution of glucomannan can form a transparent thin layer. Glucomannan is polymer that can crystallize and form the structure of fine fibers (Xu et al., 2007). This is evidenced in the observation, when glucomannan reacted to water it can form gel solution. The structure of glucomannan is very long. Pineapple fruit extract has glucosidase which can hydrolyse partially long chain structure of glucomannan (Chen et al., 2016). The process of hydrolyse partially of glucosidase from glucomannan is shown

in Figure 3. It also can be conducted by papaya leaves extract. Porang hard capsule with pineapple fruit (Figure 2c) or papaya leaves extract (Figure 2d) have glossier and smoother surface than without the extract addition. The appearance of porang hard capsule in absence and presence of pineapple fruit or papaya leaves extract are similar with commercial gelatin hard capsule (Figure 2a).

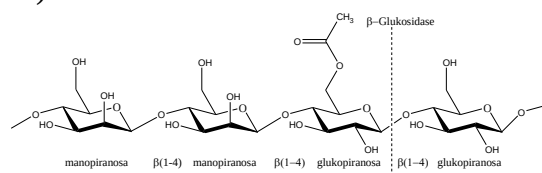


Figure 3. Hydrolyze partially of glucosidase bond from glucomannan structure.

Characteristic of hard capsule can be shown from its viscosity value. The viscosity of the gelatin in range concentration of 1-4% are very low and difficult to form a gel. Whereas, the viscosity of glucomannan were higher than gelatin in all range concentration (Table 1). The viscosity value will increase with increasing concentration of glucomannan. It indicates that the more glucomannan dissolved, the longer polymerization chain is formed so that the gel solution becomes thick. From Table 1, we use 4% glucomannan to form it become hard capsule. Decreasing viscosity value will be occurred in the addition of papaya leaves or pineapple fruit extract in glucomannan gel solution. It can be found in Table 2 and 3.

Table 1. The viscosity of glucomannan gel without addition of papaya leaves or pineapple fruit extract compare to gelatin in various concentration

Sample	Viscosity (cP)			
	1%	2%	3%	4%
Gelatin	19.98 ± 0.07	20.07 ± 0.04	20.35 ± 0.04	20.46 ± 0.12
Glucomannan Gel	32.5 ± 0.05	2049.75 ± 0.16	8007.89 ± 0.17	11373.75 ± 0.56

Table 2. The viscosity of glucomannan gel with addition of papaya leaves or pineapple fruit extract in variation of temperature

Sample	Viscosity (cP)		
	30°C	40°C	50°C
Papaya leaves extract addition	11221.02 ± 0.68	11097.14 ± 0.85	10754.37 ± 1.47
Pineapple fruit extract addition	427.08 ± 2.49	290.46 ± 2.07	139.81 ± 2.11

Table 3. The viscosity of glucomannan gel with addition of papaya leaves or pineapple fruit extract in various time

Sample	Viscosity (cP)				
	10 min	20 min	30 min	40 min	50 min
Papaya leaves extract addition	10261.74 ± 0.45	10001.68 ± 0.44	9793.61 ± 0.24	9277.47 ± 0.94	8681 ± 1.63
Pineapple fruit extract addition	875.58 ± 2.49	568.99 ± 1.74	372.11 ± 2.42	326.34 ± 2.07	286.55 ± 1.05

Hard capsule was made to cover the smell and the bad taste of drug when it consumed. Hard capsule can also be used to protect the active compounds of the drug from air and outside contaminants. Therefore, hard capsule as a drug carrier material must be able to withstand water. If the hard capsule is easily dissolved or damage toward water, then the drug will

easy to dissolve once it reaches the mouth and will cause a bitter taste of the drug. The solubility test of hard capsule was studied to observe the solubility of porang hard capsule towards water. The solubility standard for commercial gelatin hard capsule according to Kapsulindo Nusantara is more than 15 minutes.

Table 4. Comparison of hard capsule solubility test from porang with and without addition of papaya leaves or pineapple fruit extract in water at various temperature

Hard capsule sample	Solubility in water (min)		
	30°C	40°C	50°C
Commercial gelatin	19'15"	-	-
Porang without extract	20'25"	-	-
Porang with papaya extract	24' 51''	36' 59''	28' 58''
Porang with pineapple extract	19' 28"	25' 43"	34' 37"

Table 5. Comparison of hard capsule solubility test from porang with and without addition of papaya leaves or pineapple fruit extract in water at various time

Hard capsule sample	Solubility in water (min)				
	10 min	20 min	30 min	40 min	50 min
Porang	21'50"	-	-	-	-
Porang with papaya leaves extract	36'17"	38'55"	35'17"	45'00"	48'21"
Porang with pineapple fruit extract	24' 22"	20' 12"	19' 20"	25' 13"	31' 46"

Table 4 and 5, shows that all porang hard capsule with and without papain leaves or pineapple fruit extract are able to withstand for more than 15 minutes. It means that the entire porang hard capsule compatible to Kapsulindo Nusantara standard. The solubility time of porang hard capsule with and without papain leaves or pineapple fruit extract are slightly higher than the commercial gelatin hard capsule because of the thickness of the hard capsule. However, the addition of papaya leaves or pineapple fruit extract not give a significant effect on the solubility time due to the difference hard capsule thickness during the moulded process that cause the ability of hard capsule to absorb water differently.

Another important condition that must be possessed by hard capsule is easily absorbed or metabolized by the body. When the hard capsule is consumed and swallowed by the body, the hard capsule will move towards the stomach. In the stomach, the hard capsule must be able to swallow and release the drug in acid conditions. Therefore, the solubility test of hard capsule was also studied towards acid solution. The solubility standard for commercial gelatin hard capsule according to Indonesian Ministry of Health is less than 5 minutes. Table 6 and 7, shows that porang hard capsule have a similar solubility in acid solution

Table 6. The solubility test of hard capsule from porang with addition of papaya leaves or pineapple fruit extract in acid solution at various temperature

Sample hard capsule	Solubility in acid (min)		
	30°C	40°C	50°C
Commercial gelatin	3'09"	-	-
Porang without extract	1'43"	-	-
Porang with papaya leaves extract	3'05"	4'07"	3'50"
Porang with pineapple fruit extract	10' 05"	11' 16"	10' 32"

Table 7. The solubility test of hard capsule from porang with addition of papaya leaves or pineapple fruit extract in acid solution at various time

Sample hard capsule	Solubility in acid (min)				
	10 min	20 min	30 min	40 min	50 min
Porang with papaya leaves extract	3'50"	4'26"	2'47"	4'07"	2'00"
Porang with pineapple fruit extract	11' 36"	12' 34"	10' 47"	13' 09"	14' 15"

CONCLUSIONS

Porang (*Amorphophallus oncophyllus*) could be utilized as alternative plant-derived material to produce halal hard capsule. Papaya leaves and pineapple fruit extract could be added to improve the characteristic of halal hard capsule from porang. The solubility test shows that the hard capsule with both extract have a better results compared the hard capsule from porang without extract addition and gelatin hard capsule. It also proved that the extract give a better result to fabricate halal hard capsule from porang.

ACKNOWLEDGEMENT

The authors are grateful to KEMENRISTEKDIKTI (Ministry of Research, Technology and Higher Education of the Republic of Indonesia) for supporting the research funding of this work under project scheme of Penelitian Terapan Unggulan Perguruan Tinggi (PTUPT).

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