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Formulation of corn cobs hemicellulose microparticles and its characterization

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ABSTRACT

Hemicellulose is a component of Non-Starch Polysaccarides (NSP) contained in agricultural byproduct and can be separated from the other components. Hemicellulose have glucomannan as natural polysaccharides possessing the highest viscosity and waterholding capacity. Objective of this research is isolation and formulation of corn cobs hemicelluloses microparticle by gelatine ionic using tri poly phospat and characterization of corn cobs hemicelluloses microparticles. This research is done by isolation of hemicellulose and hemicellulose manufacturing of microparticles by ionic gelatine method using Tri Polyphospat (TPP) as a cross linker and microparticles characteristics was done by the solubility, infra red spectrophotometry (FTIR), high performance liquid chromatography (HPLC) with column Shim - pack VP - ODS (4.6 x 250 mm) using a UV - Vis detector at a wavelength of 280 nm with an isocratic elution system in aquabides solvent and a flow rate of 0.8 mL/min and conducted testing of the morphology of the microparticles. The results showed that the microparticles of hemicellulose can be made using corn cobs that have solubility in alkaline conditions, has the characterization by FTIR , HPLC and the results of SEM and PSA is in the range of 6 to 200 nm. This research concluded that corn cobs can be used as raw material for the manufacture of hemicellulose microparticles by using TPP as a crosslinker.

Keywords: formulation, Cross linked, hemicelluloses, micro particles,. FTIR and HPLC

INTRODUCTION

Hemicelluose is a biopolymer as polysaccharide that belongs to non-starch polysaccharide (NSP), present abundantly as agricultural by product. Hemicellulose is a hetero- polysaccharides since it is composed of more than one kind monosaccharides mainly glucose, galactose, mannose, glucoronic acid, fructose etc. Such a composition resulted in different hemicellulose of different in solubility, size of polymer. Galacto-mannose, Xylane, and Gluconxylane found to be polysaccharide that is slightly soluble in water, where as the one soluble in water are glucose, galactose, arabino-xylane etc. To increase the economic value of hemicellulose, effort should be made to isolate or separate it from other component for example cellulose, lignin those coexist in plant, so that it can be utilized as a new alternative polymers for various applications especially in pharmaceutical preparations [1].

Hemicellulose is bound to the surface of cellulose microfibrils are complex polysaccharides which themselves do not form micro fibrils. These bound polysaccharides can be extracted from the plant cell wall with the aid of strong alkali. Glucomannan is monomer of hemicelluloses are mainly a straight-chain hydrocolloidal polysaccharide of the mannan family with about 8% branching through β-(1→6)-glucosyl linkages. The component sugars are β-(1→4)-linked D-mannose and D-glucose in a ratio of 1.6:1 which may differ depending on the source [1].

In the pharmaceutical industry, both natural and synthetic polymers have been largely used with different applications for the development and production of cosmetics and traditional dosage forms and novel drug delivery systems. For instance, a hemicellulose in the pharmaceutical are used as fillers, lubricants, disintegrants, binders,

glidants, solubilizers, and stabilizers in tablets, capsules, creams, suspensions or solutions. Additionally, biodegradable and bioadhesive polymers may play an important role in the development of novel drug delivery systems, especially for controlled drug release. Controlled drug delivery technology represents one of the border areas of science, which involves multidisciplinary scientific approach, contributing to human health care. In addition, several important applications of hemicellulose have been done by making the derivatives which have pharmacological effects such as lowering cholesterol, and inhibitors of HIV [2-7].

Natural polysaccharides, as well as their derivatives, represent a group of polymers that are widely used in pharmaceutical formulations and in several cases their presence plays a fundamental role in determining the mechanism and rate of drug release from the dosage form. These naturally occurring polymers have been employed as excipients in the pharmaceutical industry in the formulation of solid, liquid and semisolid dosage forms in which they play different roles as film formers, matrix formers or release modifiers, thickeners or viscosity enhancers, emulsifiers, suspending agents and muco adhesives. Specifically, they have been used in the formulation and manufacture of solid monolithic matrix systems, implants, films, beads, microparticles, nanoparticles, inhalable and injectable systems as well as viscous liquid formulations [5-8].

The concept of drug targeting and controlled drug delivery is used in attempts to improve the therapeutic index of drugs by increasing their localization to specific organs, tissues or cells and by decreasing their potential toxic side effects at normal sensitive sites [8-9].

Polymeric microparticles have been studied and developed for several years. Their contribution in the pharmacy field is of utmost importance in order to improve the efficiency of oral delivery of drugs. As drug carriers, polymer-based microparticles may avoid the early degradation of active molecules in undesirable sites of the gastrointestinal tract, mask unpleasant taste of drugs, reduce doses and side effects and improve bioavailability. Also, they allow the production of site-specific drug targeting, which consists of a suitable approach for the delivery of active molecules into desired tissues or cells in order to increase their efficiency. The component sugars may contain acetyl side branches on some of the backbone units which contribute to the solubility and swelling capacity of the glucomannans. The acetyl groups consequently enhance the solubility of the glucomannans as natural polysaccharides possessing the highest viscosity and waterholding capacity. Konjacglucomannan has been investigated as an effective excipient in controlled release drug delivery [9-14].

The aim of this work is to extracted of hemicellulose from corn cobs, which presents a promising and the development of microparticles based on hemicelluloses and prepared by cross linked methods for alkaline target sitecarrier. Physicochemical characterization of the polymer regarding FTIR, HPLC, scanning electron microscope (SEM) and Particle size analysis (PSA) of microparticle size.

MATERIALS AND METHODS

Apparatus Magnetic Stirrer, hot plate, universal indikator, Filter membran PTFE @100, Centrigfuge, pH meter, Homogenizer, Particle size analyzer, Viscometer, thermostate, microscope, scanning electron microscope, FTIR (Hitachi) HPLC (Shimadzu) Spektrofotometri UV (Hitachi), microscope transmisi electron,

Material and Reagent Corn Cobs were obtained from local corns in Medan, Indonesia. NaOH (E.Merck), 35% hydrogen peroxide (E.Merck), 96% ethanol (E.Merck), 98%acetic acid (E.Merck), propylene glycol (E.Merck), and all other chemicals used were of analytical grade.

Isolation of Hemisellulose from Corn Cobs

The corn cobs powder of 50 grams was added to 500 cm3 of 0.1 M NaOH in 70% ethanol and heated at 60°C, then stirred for 2 hours to dissolve the lignin. The suspension was allowed to cool to room temperature and filtered through Whatman filter paper. The precipitate was added 500 cm^3 of 0.2 M NaOH and stirred for 8 hours at room temperature to dissolve hemicellulose, and then filtered. The filtrate was heated at a temperature of 65°C, and added 137 cm^3 of 3% H_2O_2 in stages. Each addition of 1 cm3 3% H_2O_2 to the filtrate was stirred constantly. Stirring was performed until the entire 3% of H_2O_2 was used and continued to a clear solution. Solution of 10% acetic acid in 95% ethanol with a ratio of 1:4 (v/v) was added to the sample solution and left at room temperature for 6 hours until the precipitate was formed. The suspension was centrifuged at a rate of 10.000 rpm for 15 minutes, and the filtrate was discarded. The precipitate was washed with 96% ethanol, and dried in vacuum dryer. The washed precipitate is hemicelluloses [15].

Preparation microparticles of hemicelluloses using tri poly phospat as cross linker

1. One gram of corncob hemicellulose and then diluted with 0.1 N NaOH until dissolved, to 100 ml. the obtained solution 1% hemicellulose.
2. One gram of corncob hemicellulose and then dissolved with 0.1 N acetic acid to 100 ml of the obtained suspension hemicellulose in acetic acid.
3. 10 ml suspension of hemicellulose in 0.1 N acetic acid was added hemicellulose in 0.1 N NaOH solution to pH 7 then the turbid solution is formed and left to precipitate fine.
4. To the turbid solution was added 1 ml of propylene glycol and centrifuges until it forms a viscous solution.
5. Sodium tripolyphosphate (TPP) weighed 3.3 grams, then dissolved in water till 100 ml of the obtained solution 0.33% TPP.
6. The hemicellulose viscous solution was added through a dropwise TPP solution while stirring with a magnetic stirrer for 30 minutes and then allowed to stand 24 hours and visually observed gel is formed.
7. The gel is formed and then poured into a thin s lab to form a thin film layer of light brown and dry at cool temperatures to obtain a thin layer of dry; milled until smooth then obtained fine particles [8-14].

Characterization of Corn Cobs Hemicellulose Using Infrared Spectrophotometry (FTIR)

Method of characterization by High Performance Liquid Chromatographi as follows: 25 mg of hemicellulose weighed, and then put into 50 ml volumetric flask and added pure water to mark. Shaken, then filtered (first few ml of filtrate was discarded). Solution was then filtered through a membrane filter of 0.2 μm Cellulose Nitrate. Then about 100 ml solution was injected into the HPLC system via a loop injector with a 20 ml, using an isocratic elution system with distilled water with a mobile phase, flow rate 0.8 ml / min. The detection was made using a UV detector at a wavelength of 280 nm. The chromatogram recorded and performed a qualitative analysis by the area, peak height and retention time corn cobs hemicelluloses [15].

Characterization of Corn Cobs Hemicellulose Using HPLC

Identification is performed by HPLC is a modification identification by [16] the corn cob hemicellulose and hemicellulose micro particles with the use of a difference detector is a refractive index, while the identification is used UV light detector.

Characterization of hemicelulose microparticle Using SEM

Particle surface morphology from hemicelulolse particle and hemicellulose micropartcles is done by scanning electron microscopy.

Characterization of hemicelulose microparticle Using PSA

Particle size analysis from hemicelulolse particle and hemicellulose micropartcles is done by particle size analyzer

RESULTS AND DISCUSSION

Isolation of Corn Cobs Hemicellulose

Isolation of the isolation process carried out at alkaline pH with NaOH at soaking time of each procedure ranged from 8 hours to 16 hours. Yet, immersion does not affect the hemicellulose because the hemicellulose does not break down into their constituent monomers in alkaline conditions. In the isolation process, the addition of acids used to precipitate hemicellulose, whereas the addition of ethanol is to increase the amount of hemicellulose which precipitates or clumping, making it easy to separate from the solution because hemicellulose is not soluble in acid and ethanol [14]

Important factor influencing the hemicellulose content of each procedure is delignification process, because some isolation procedures for delignification using different materials such as chlorine or H_2O_2 in alkaline atmosphere. The delignification is conducted again after the isolation process. The second delignification process is done with 3% H_2O_2. The use of 3% H_2O_2 in the modified isolation method conducted by the researcher aimed to produce more white hemicellulose, in addition to the waste generated does not produce dioxins so there is no damage the health and pollute the environment [14].

Preparation of Corn cobs Hemicellulose Microparticles

Preparation of the hemicellulose microparticles made at pH 7 by mixing a solution of 1 gram of hemicellulose in 0.1 N NaOH 40 ml and a solution of 1 gram of hemicellulose in 0.1 N acetic acid 40 ml and the mixing is done by adding slowly hemicellulose in NaOH while stirring and the pH checked with a pH meter to obtain a pH of 7. Then the suspension solution pH 7 added 1 ml propylene glycol and let stand for 24 hours while stirring. And the gel solution is formed.

In the gel solution is added gradually 0.33% TPP solution until a solution is more viscous gel vikositasnya, then stirred for 24 hours and then create a thin film layer on top of the glass plates the size of 20 x 40 cm and let stand until dry in room temperature. Drying at room temperature lasts for 48 hours. Drying should not be above room temperature because it will change color from yellow-brown to dark brown.

The results showed that the microparticles formation hemicellulose: TPP, only be formed at a concentration of 1% hemicellulose. In this research note that in order to prevent the formation of particles in the size of the microparticles concentration of 1% hemicellulose must be in low concentrations, the micro-sized particles can be obtained and the use of TPP in very low concentrations and a very small amount. The concentration and volume ratios of critical TPP can be used are 0.33% and 5: 1, if more than that would easily form a heterogeneous microparticle size above 200 nm up to micrometer. Beside that after drying is done grinding until smooth and then examination of solubility, morphology with SEM, PSA and FTIR and HPLC, after smoothing process occurs not uniform microparticles formed and this can be seen in the results of SEM, this is the time for the grinding process is not long enough so that subtlety is not uniforms.

Table 1. Characterization of corn cob hemicelluloses and hemicelluloses micro particles with Solubility, FTIR and HPLC

Solubility	Aquadest	Poorly soluble
	Hot water	Dissolve
	1% HCl	Poorly soluble
	1% NaOH	Dissolve
FTIR	Functional groups	Hydroxyl Carbonyl Carboxylate
HPLC	Retention time	1.802
	Peak height	1.06418
	Area	5.11558
	Symetric	0.82

Table 2. Characterization of corn cob hemicelluloses microparticles with Solubility, FTIR and HPLC

Solubility	Aquadest	Poorly soluble
	Hot water	Dissolve
	1% HCl	Poorly soluble
	1% NaOH	Dissolve
FTIR	Functional groups	Hydroxyl Carbonyl Carboxylate
HPLC	Retention time	1.79 and 2.024
	Peak height	1.06418 and 2.22
	Area	5.11558 and 2.0728
	Symetric	0.82 and 0.79

Identification by FTIR

Identification of the infrared the corn cobs' hemicellulose and hemicelluloses microparticles provide the following Figure 1 and2 below

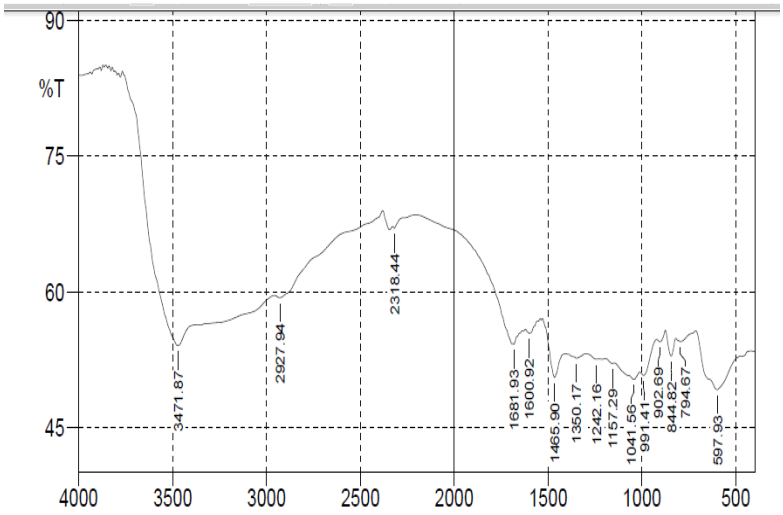

Figure 1. FTIR of corn cobs hemicelluloses

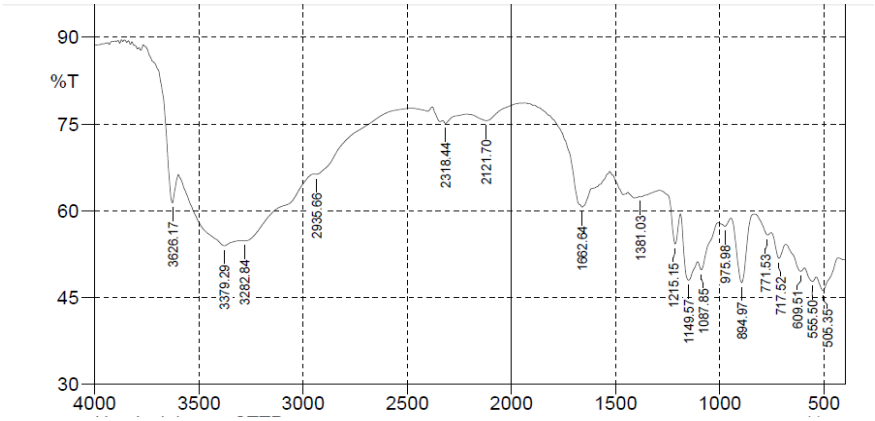

Figure 2. FTIR microparticles of corn cobs hemicelluloses

Based of Figure 1 and Figure 2 can be seen that FTIR of hemicellulose and hemicellulose microparticles show different vibration due to the additions and changes in vibration on micro particles, it proves the existence of structural changes due to the inclusion of TPP in the manufacture of hemicelluloses microparticles

Identification Corn Cobs Hemicelluloses microparticles by HPLC

Identify chromatogram of corn cobs' hemicellulose with HPLC by using a C18 column with solution of distilled water with flow rate 0.8 mL/min and the detector Ultra Violet rays at a wavelength of 280 nm

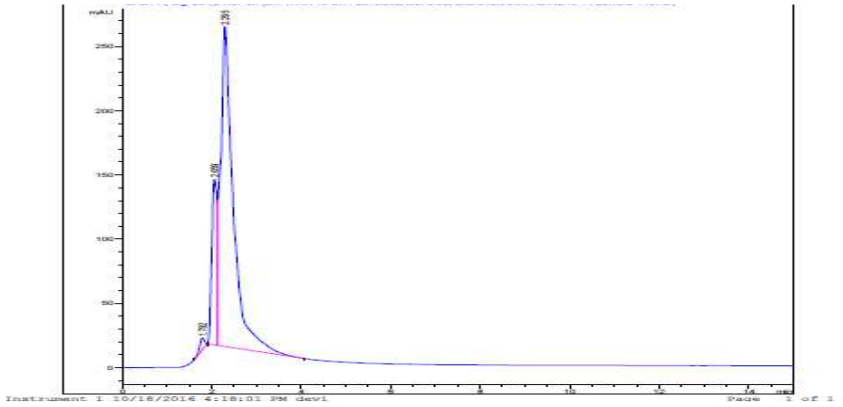

Figure 3 Chromatogram of corn cobs hemicellulose particle with HPLC

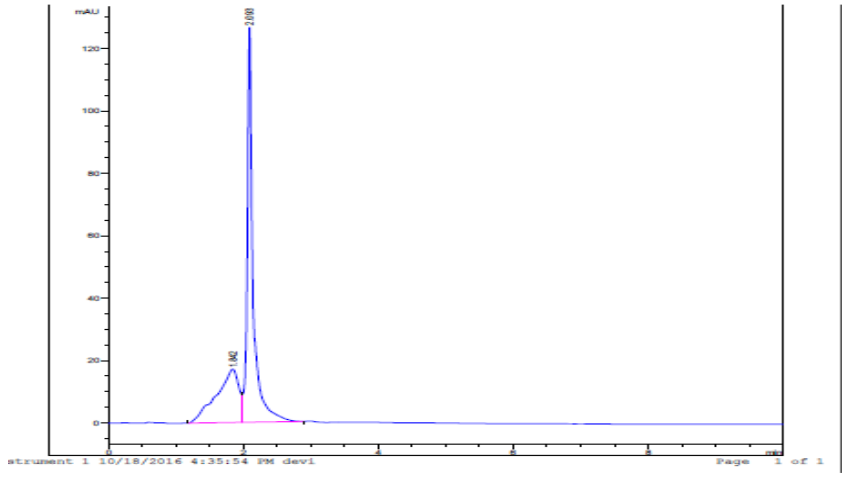

Figure 4 Chromatogram of corn cobs hemicellulose microparticles with HPLC

The identification of HPLC chromatograms is done by aquabidest as the mobile phase, C18 column, and the flow rate of 0.8 ml min with UV light detector at a wavelength of 280 nm [15]. Mechanisms for identifying the

supporting components monomer of the hemicellulose using an ODS column based on the presence of hydroxy functional groups in the sample, Seen from the formed chromatogram. the two samples each have three peaks with the same retention time with the longest retention time is 1.79 minutes with the vast differences in the yield's respective areas. This means that identifying the HPLC indicates of corn cobs hemicelluloses and hemicelluloses micro particles gives the shape and area of the same peak.

Identification With SEM and PSA[16]

Identification of hemicellulose microparticles can be seen at figure below.

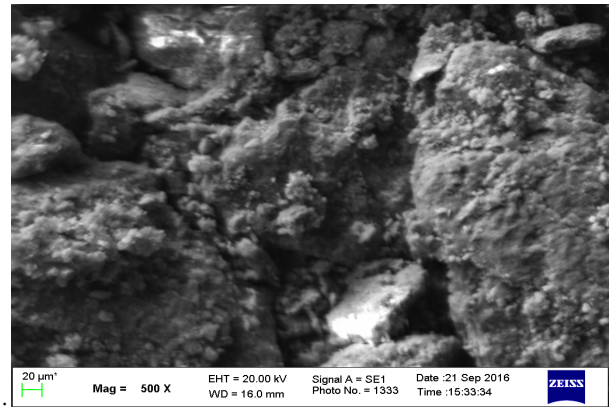

Figure 5. SEM image of hemicellulose particles

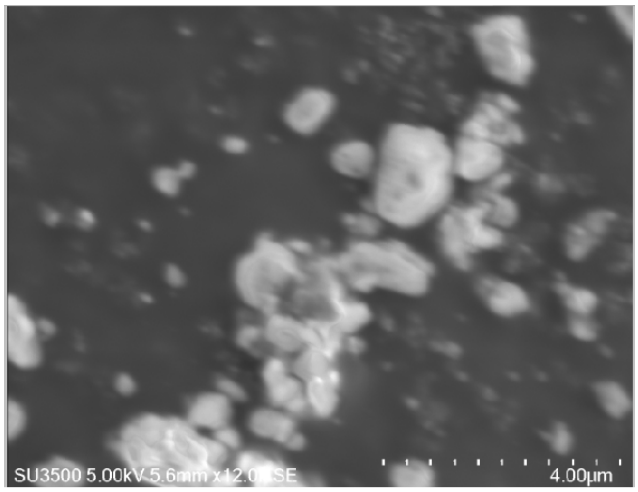

Figure 6. SEM image of hemicellulose microparticles

Based of Figure 5 and Figure 6 above can be seen that the hemicellulose analysis by electron microscopy (SEM) was conducted to determine the size, shape and surface of the particles [16]. SEM analysis results indicate that the particle hemicellulose and hemicellulose microparticles has an uneven surface. SEM analysis results showed the particle size of hemicellulose microparticles smoothed partly micro-meter scale, but its size still not uniform. In the picture can also be seen that the particles forming aggregates.

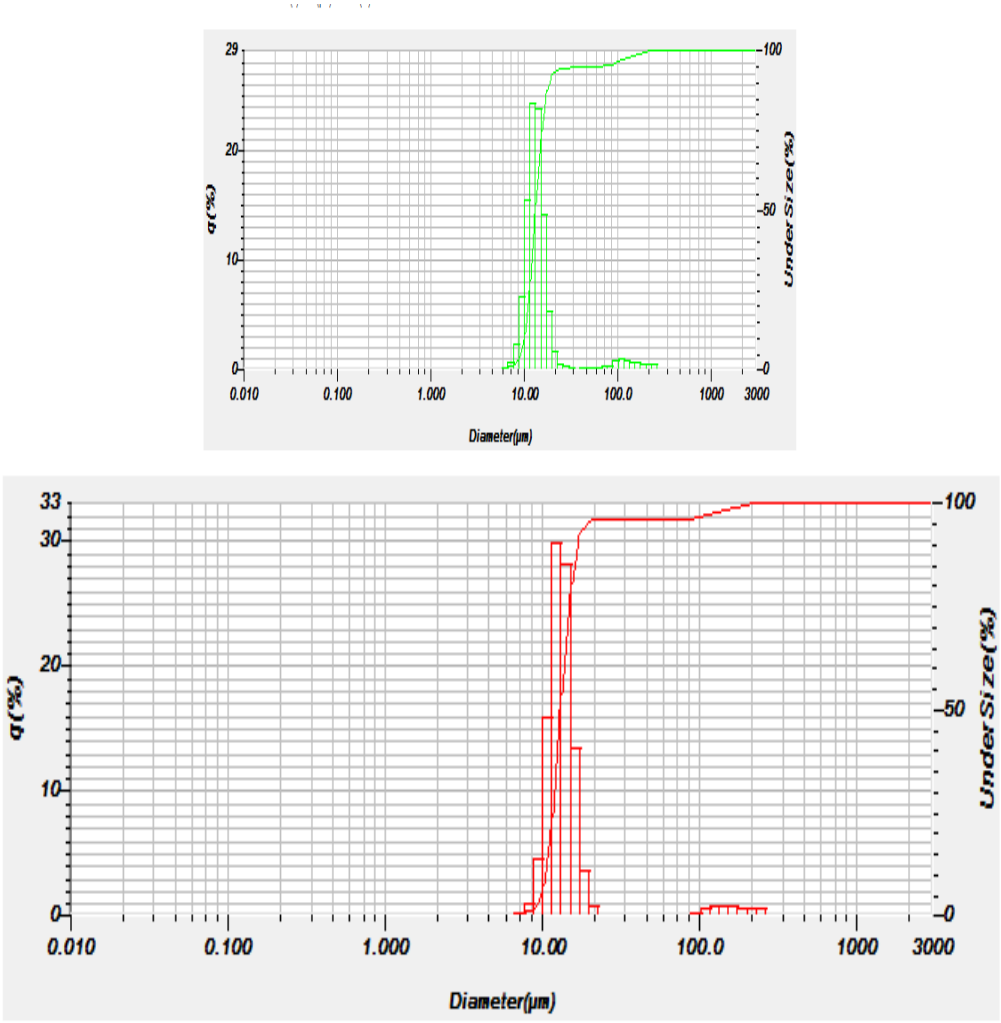

Figure 7. PSA particles of (a) hemicellulose, (b) hemicelluloses microparticles

Based of Figure 7a and 7b above it can be seen that the results of the hemicellulose and hemicellulose microparticles, which has been acquired subsequently comminuted, then evaluated particle size distribution with LA 950 laser scattering particle size distribution analyzer. Determining the size and distribution of particles using a particle size analyzer (PSA) here performed with light scattering to measure the particle size to the micro meter micron. The result of using PSA measurements show the size and distribution of particles of a representative sample. The particle size distribution is known through the resulting graph The particle size of hemicellulose and hemicellulose microparticle in a row is in the range 6.74 to 262.38 μm with an average of 30.19 μm, and hemicellulose microparticle in a row 5.70 to 232.64 μm with an average of 17.22 μm . The test results of particle size distribution is obtained the particle size at the micrometer scale.

CONCLUSION

That corn cobs can be used for the manufacture of micro-particles by using TPP as a cross junction and has FTIR and HPLC test-specific and based on the solubility of the micro-particles can be used as a slow release of the drug under alkaline conditions.

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