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Preparations of Nanoparticle Caffeine Extracted From Tea (Camellia Sinensis)

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ABSTRACT
Caffeine from Tea (Camellia sinensis), considering as topical used in the future for multi propose. In the manufacture of caffeine nanoparticles using ingredients form Tea extracted process using digestive method, to obtain caffeine. Then the caffeine is made into a formulation of polylytic nanoparticles PLGA CHITOSAN and PVA. In the process of nanoparticle formulations is used emulsion solvent evaporation method. The formulation of caffeine nanoparticles is characterized by particle size PSA, zeta potential and morphology is performed by using SEM. Elucidation with FTIR, HNMR and CNMR and HPLC. Overall, microfluidics produced complexes with improved characteristics such as lower polydispersity index (PDI ~ 0.2) and mean size (~200 nm). Chitosan (HC) contributed to an even smaller size and PDI value of the complexes. Caffeine could also be encapsulated in complexes, the highest encapsulation efficiency was achieved (~70%). HNMR and CNMR, FT-IR Confirm to standard caffeine (Merck).

Keywords : Nanoparticle, extract caffeine, PLGA-PVA. Tea, PSA

I. INTRODUCTION

Tea (Camellia sinensis) is both a plant and a foodstuff. Many bioactive compounds, which are present in the final tea product and related to its quality or functional properties, are produced during the tea manufacturing process.[1] Tea are the second most important ingredient in the world after oil. Tea has a higher caffeine content of Camellia sinensis. The caffeine content from Tea is varies depending on the type of Tea, originally, and how to roast and how it to be processed.[2,3] Tea is the second most popular drink after coffee water and is consumed worldwide, with a daily consumption of about 1.6 billion cups. This is because caffeine is believed to be able to increase concentration, memory, and mind.[4,5] Indonesians, as many as 31.5% has consume caffeinated beverages at least once a day.[6] Caffeine intake per person should not exceed 150 mg per day. As per SNI 01-7152-2006, the caffeine limit is 150 mg per day and 50 mg per serving. However, if you consume 100mg of caffeine per day, this can lead to caffeine addiction. To keep the concentration of caffeine constant in the skin or into the plasma, it is necessary to be made in nanoparticles scale depend on drug used for the skin propose using polymers so that caffeine is released slowly so that it can last a long time and have a long effect as expected.[7] Caffeine is being increasingly used in cosmetics due to its high biological activity and ability to penetrate the skin barrier. This alkaloid is frequently used as a hydrophilic model substance in human and animal skin penetration as well as different synthetic membrane using Franz diffusion cell experiments. The commercially available topical formulations of caffeine normally contain 3% caffeine. As for a cosmetic purpose, caffeine is used as an active compound in anti-cellulite products because it prevents excessive accumulation of fat in cells. This alkaloid stimulates the degradation of fats during lipolysis through inhibition of the phosphodiesterase activity. Caffeine has potent antioxidant properties. It helps protect cells against the UV radiation and slows down the process of photoaging[1] of the skin. Moreover, caffeine contained in cosmetics increases the microcirculation of blood in the skin and also stimulates the growth of hair through inhibition of the 5-α-reductase activity.[8]

Currently there have been studies of nanoparticles using polymer systems that are able to increase the bioavailability of drugs, for example in the research of amoxicillin-based polymer nanoparticles that show the results that the use of this polymer is able to control drug release, increase the solubility of bioactive drugs, make

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them more stable in the gastrointestinal (GI) tract, and suitable for oral administration < 100 nm. This process uses a nanotechnology system which will involve the synthesis of particles from nanoparticles ranging in size from 20-200 nanometers and this is also now widely used in the food, pharmaceutical and cosmetic industries.[9]

Nanoparticles vary in size, but typically range from 100 to 500 nanometers. With these nano particles capable of delivering drugs to specific tissues, allowing controlled treatment, the drug will precisely hit its target thereby reducing the toxicity caused by the drug.These nanoparticles can also increase patient adherence to taking the drug because with these nanoparticles are able to make the drug awake levels for a long time so that the patient does not need to repeat the dose at any time.[10]

There are many reasons why the use of nanoparticles is important for the advancement of therapeutic, cosmetics and diagnostic drug delivery. On the one hand, oral and injectable traditional medicines today are not necessarily designed with the correct prescription for each of its products. Polymer-based nanoparticles can increase the bioavailability of targeted drug delivery and controlled drug delivery. By modifying the system, internal enzymes can prevent drug damage.[11] The purpose of the study was to synthesized and characterized caffeine nanoparticles that extracted from Tea. Tea (Camellia Sp var.) from Pagar Alam of South Sumatra Province, is one of the best Tea in Indonesia.

II. MATERIAL AND METHOD

MATERIAL

Tea (Camellia sinensis), Ethyl acetate, Sigma, Distilled water, Na_2CO_3 (Sigma), PLGA- , Poly(D,L-lactide-co-glycolide) Resomer® RG 752 H Sigma Aldrich, PVA Poly(vinyl alcohol) Cat-341584 Sigma Aldrich, Chitosan, Pb Acetat (E-MercK), Chloroform E-MercK, Acetone E-MercK, aqua for injection.

Erlenmayer, rotary evaporator, paper filter, spatula, glass beaker, vial, magnetic stirrer, Capiller tube, Plate TLC, PSA (Particle Size Analyzer) HORIBA SZ-100, mikroscope elektron transmision (TEM Jeol 1010), analytic balance , hot plate, sonicator bath, micro pipet,

SAMPLE COLLECTION

Tea (Camellia sinensis) from Pagar Alam (Brand Market) , South Sumatra Province, Indonesia,. The fine powder Tea is ready for extraction.

EXTRACTION

Tea powder 50 Gram is extracted by a digestion process 250 mL with in aquadest. The Tea are mixed with distilled water and heated and then filtered using filter paper and the filtrate is added with Na_2CO_3 then heated again and filtered again by using a paper bag and fractionated using Pb acetate 10 %. Filtered and add 10 % sulfuric acid to precipitated the excessive metally of Pb. Finally filtered and extracted by chloroform for three times repetitions. The chloroform extract obtained was evaporated using an evaporator to produce a thick extract and dried to produce caffeine powder.

SAMPLE PREPARATION

PVA solution is made by weighing PVA powder as much as 250 mg and then dissolved in 10 mL with aqua pro injection at a temperature of 60°C. The mixture was then stirred for 24 hours, speed 100 rpm to produce a clear and homogeneous.

PLGA solution, is made by weighing 100 mg of PLGA powder, dissolved in 0.5 mL of ethyl acetate and homogenized using a stirrer for 4 hours, speed 175 rpm at room temperature.

Caffeine, crystal powder was weighed 50 mg and dissolved with 2 mL of ethyl acetate then homogenized and stir with 175 rpm for 4 hours.

Nanoparticle Caffeine PLGA-PVA Formulated

To have nanoparticle caffeine we used suspension method. The manufacture of nanoparticles was carried out using PLGA polymer and PVA emulsion solvent evaporation method. A total of 2 ml of the caffeine solution was then added with 0.5 ml of PLGA solution mixed using a magnetic stirrer at an oil phase speed of 750 rpm. The solution was pipetted and dripped by drop into the aqueous phase, 2,5 mL of PVA solution and stirred for 1 hour at a speed of 750 rpm The process was continued by homogenizing the suspension using sonication for 5 minutes with a wave power of 42 kHz. In the final stage, 50 mL of distilled water was added, then followed by the evaporation process organic solvent by stirring for 24 hours to produce a suspension.

CHARACTERISITIC NANOPARTICLE

The caffeine nanoparticles preparation were characterized by using PSA (Particle Size Analyzer) to determine of diameter, PDI and Zeta Potential. This test uses a PSA brand Horiba SZ-

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100 with the dynamic light scattering (DLS) method. The process is by taking 50µL of nanoparticle suspension and diluting it using distilled water in a ratio of 1:100 then inserting it into a 50µL PSA cuvette and then the PSA tool will shoot monochromatic light which will be captured by the detector so as to produce the PDI value, diameter and zeta potential of the nanoparticle

MORPHOLOGI DETERMINE PARTICLE

The morphology was observed at 30.000x using a Scanning Electron Microscope (SEM) with a voltage of 80.0 kV

HNMR and CNMR PREPARATION

Amount of 50 mg sample dilute in 1 mL acetone (d6) for HNMR , proton , 10 mintes, JEOL series. 500 Htz, Single pulse. Amount of 50 mg of sample dilute in (d6) for CNMR, Carbon, 2 hours, Single pulse, 500 Htz.

III. RESULT

The size of nanoparticles resulting with an average diameter is 182,3 nm. The zeta potential measurement have an surface charge of -14.6 mV. The size distribution observed with the poly density index (PDI) value obtained was 0.150. PSA, PDI and Zeta Value data can be seen in Table 1.

Table 1. Characteristic of Nanoparticle Caffeine PLGA-PVA Formulated

Characteristic	Value
Particle Size (nm)	182,3 nm
PDI	0,254
Zeta Potensial (mV)	-14,6

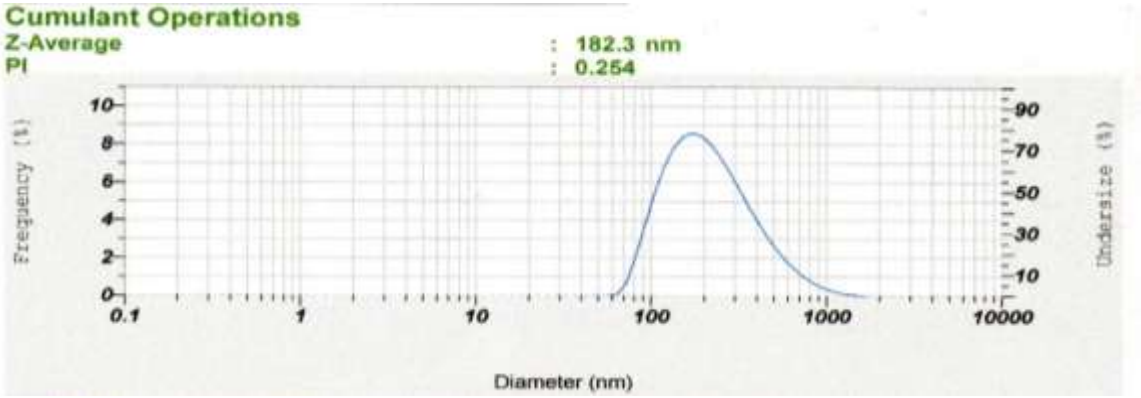

Figure 1. Nanoparticle size of Caffeine PLGA-PVA Formulated

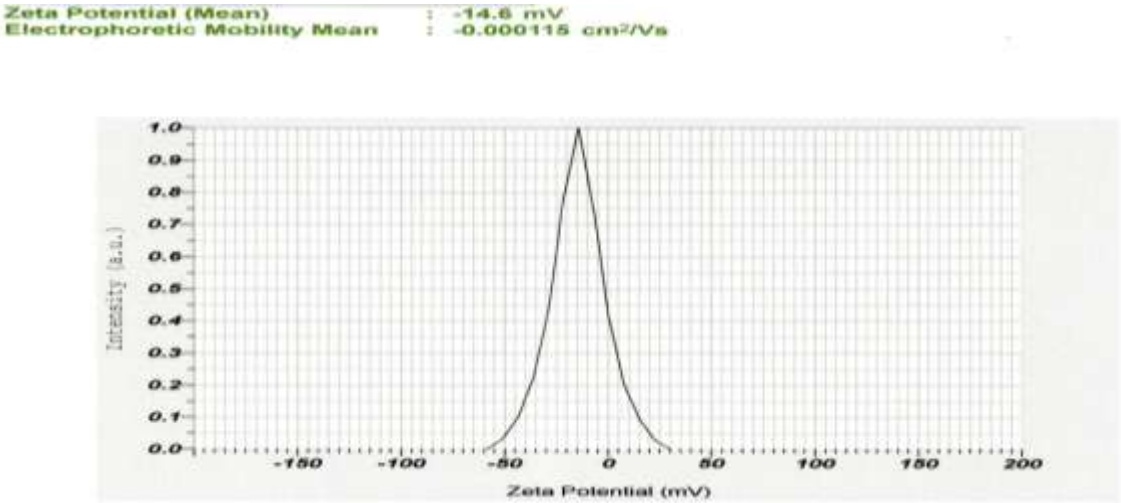

Figure 2 Zeta Potensial nanoparticle of caffeine formulated PLGA-PVA

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Characterization using Scanning Electron Microscope (SEM) aims to see the surface morphology of nanoparticles. The surface characterization of the nanoparticles at 30,000x magnification showed that the surface of the caffeine nanoparticles was as normal (Not showed in this article).

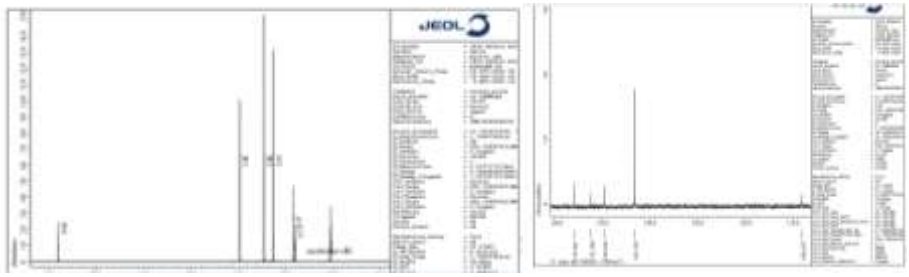

Figure 3 Data H NMR and C NMR of Caffeine

Data proton HNMR and C^{13} NMR of caffeine nanoparticle preparation have a similarly to data caffeine standard. The shift proton HNMR were showed in 3,996 ppm ; 3,456ppm; 2,87ppm; 2,804 ppm. Specific to caffeine 1,3,7 Tri methyl xanthine.

Data C^{13} Carbon NMR of caffeine nanoparticle preparation showed carbon in 155,9ppm; 152,3 ppm; 149,62 ppm; and 143, 22 ppm . Those carbon similar to caffeine CNMR standard (Figure 3).

Data of Efficiency % EE.

To calculate efficiency, % EE is used 20, 40, 60, 80, and 100 ppm respectively concentration of caffeine preparation to have based curve.

CODE	Sampel	Supernatan	% EE
R1	27,51603	8,886635	67,7
R2	27,61271	8,882758	67,8
R3	27,68461	8,885879	67,9

Extrapolated to sample refer to nanoparticle we have ~67.8 % EE .

IV. DISSCUSSION

Caffeine is being increasingly used in cosmetics due to its high biological activity and ability to penetrate the skin barrier. This alkaloid is frequently used as a hydrophilic model substance in human and animal skin penetration as well as different synthetic membrane.[16,17] Need to pursuit the effect of caffeine in many purposed. Caffeine has many Particle size information it is important due to the manufacture of nanoparticle formulations, where the smaller the particle size, the better the drug release power. Particle size is one of the factors that affect the efficiency of the compound or drug. Small in size (nano size) can help the drug distribution process reach its target. Nano size also has high solubility and absorption efficiency. From the results of the particle size is 182,3 nm (Figure 1), which means that it is in the nanoparticle size range used as topical propose because it is known that nanoparticles >200 nm. Nanoparticle size ranges for topical propose can be from 100 to 500 nm. In this study particle size is obtained, between 200-500nm nm which means that caffeine PLGA –PVA formulated perform in nanoparticle size. In this study the zeta potential test, a value of -10,3mV was obtained and this indicated that the suspension was stable because nanoparticles with a zeta potential value of less

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than -30 mV and greater than +30 mV had higher stability (Figure 2).[17]

PDI assessment is perform to see whether or not the size of a particle is uniform and from the test results obtained a PDI value of 0.148, this means that the distribution is homogeneous because it is close to a value of 0 where if the value is 1 it indicates a very wide size distribution and contains large particles and can undergo sedimentation (**Table 1)**. In terms of morphology,[18] the surface shape look normal, this indicates that the drug is well coated and the release power will be slow and it will make it easier for the drug to be given via a certain mode because in drug delivery systems that use particles as conductors such as micro particles, the ability to coat drugs is high with small particle sizes, and a uniform spherical shape is preferable.[19] This will facilitate the administration of drugs through certain routes such as intravenous, intranasal and other.[20,21]

The particle size test was performed for the sample that had passed the evaluation phase with good stability of the preparation. The PDI value of sample is measured at 0.254. This value refers to the distribution of the particle size. If the PDI value is close to 0, the dispersity of the particle size is homogenous. If the PDI value is greater than 0.5, the heterogeneity is considered high. Samples with a PDI value greater than 0.7 have a very wide size distribution. This signifies that the size of the sample has a homogenous particle size dispersion. PDI measures the homogeneous of nanoparticles, the smaller the pdi the more homogeneous nanoparticles. Nanoparticles with pdi smaller than 0.4 is considered acceptable for drug deliver. This is because differences among particle sizes are impactful on particle characterization. The result of PSA revealed that the particle size is 182.6 nm. Considering this, it fits the characteristic of an acceptable where the nanoparticle size ranges from 200 to 500 nm is better depend on the drug design using for topical as cosmetics.[22] Fit and good enough 70 % EE drug release from encapsulated refer to study literature [23,24].

V. CONCLUSION

Its has been successfully to have caffeine nanoparticles from Tea extract, formulated by using PLGA and PVA and Chitosan polymers through the emulsion solvent evaporation method. We obtained diameter value < 200 nm, fit to zeta potential and PDI. The HNMR and CNMR fit to caffeine standard. Based on the research, the authors suggest that further research can be done to have pharmaceutical nanocaffeine formulated performance.

CONFLICT OF INTEREST STATEMENT

There is no conflict of interest regarding the submitted research article.

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