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Characterisation of Physical Properties of Curcumin Isolated from *Curcuma domestica* Val

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ABSTRACT

The compound Curcumin has many health benefits. Due to their benefits, curcumin molecules are now being developed into pharmaceuticals. However, there is a lack of information on the properties of curcumin compounds that can be used as pre-formulation data, preventing the production of pharmaceutical products based on curcuminoids. This study sought to determine and characterise the physical properties of curcumin to generate pre-formulation data for the development of curcumin-based pharmaceutical products. Differential scanning calorimetry (DSC), powder x-ray diffractometry (PXRD), scanning electron microscopy (SEM), zeta potential value measurement using a zeta potential analyzer (ZPA), tap density, proper density, and solubility tests in propylene glycol, PEG 400, glycerin, and sorbitol solvents were used to characterize the physical properties of curcumin. Curcumin has a compressibility index of 16.463%, a proper density of 1.116 g/mL, a melting point of 169.63°C, a particle morphology of long beams that are crystalline, a zeta potential value of -59 mV, and was readily soluble in PEG 400. According to the study's findings, the isolated curcumin has a long beam shape, is amorphous, incompressible, has a reasonable flow rate, is stable under heating, and does not readily agglomerate.

Keywords: Characterization, Characteristics, Curcumin, x-ray diffractometry

Introduction

Many indigenous medicinal plants prove that Indonesia has the world's second-largest biodiversity. Due to the abundance of these medicinal plants, most Indonesians, particularly in rural areas, rely on traditional herbal remedies to treat illness.[1] Based on this potential, Indonesian plants could be produced as pharmaceuticals. One of Indonesia's most productive agricultural and spice crops is turmeric. Turmeric, a natural resource that belongs to Indonesia, provides advantages in daily life in addition to being a food ingredient and traditional medicine.[2]

Curcuminoids include curcumin, desmethoxycurcumin up to 10%, and bisdemethoxycurcumin up to 1-5%. [34] and other medicinally beneficial compounds like essential oils made up of sesquiterpenes like turmerone up to 60%, zingiberene up to 25%, phellandrene, sabinene, borneol, and cineol, are found in turmeric. Additionally, turmeric includes 1-3% of fat, 3% of carbs, 30% of protein, 8% of starch, 45-55% of vitamin C, and salts of the minerals calcium, phosphorus, and iron. [5,6] Turmeron and zingiberene are the dominant compounds found in turmeric essential oil that have potential health benefits as anti-inflammatories that can help reduce inflammation, antioxidants, antimicrobials, and antifungals.[7,8] Curcumin is now being explored for the development of pharmaceutical products. There are both primary and secondary plant metabolites, and mostly, it is the secondary metabolites that exhibit pharmacological activities.

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For drug development, there is a need for the isolation of curcumin compounds from the plant material to identify the effective chemicals in the plant. [9]

The rhizomes of turmeric plants contain curcumin. Biological activities of curcumin, also known as 1,7-bis(4' hydroxy-3 methoxyphenyl)-1,6 heptadiene, 3,5-dione, include anticancer[10], anti-inflammation[11], antibacterial, antifungal, antiparasitic, anti-HIV, against Alzheimer's disease and hypercholesterolemia, anti-infective, antiproliferative, anti-fertility and for blood clotting.[12,13] Curcumin appears as short rods or crystalline prisms, is insoluble in water or produces emulsions, and is readily soluble in acetone, ethanol, methanol, benzene, and chloroform. Under UV light, these compounds exhibit fluorescence ranging from a weak reddish-orange to a solid yellow-orange colour. This fluorescence is unstable when exposed to sunlight but becomes stable when heated.[14]

Characterization of the physical properties of a chemical compound is very important for various purposes, such as characterization of compounds. In principle, the molecular structural formula of a chemical compound is a description of information about the chemical, physical, or biological properties of the compound.

Curcumin has many excellent benefits for body health, including anti-inflammatory, antioxidant, arthritis symptoms, eye health, and brain health.[15,16] It is, therefore, necessary to investigate the physical characteristics of curcumin isolated from natural sources in order to develop a good pharmaceutical product of curcumin.

The following analytical methods were used to characterize the isolated curcumin: melting point using Differential Scanning Calorimetry (DSC), crystallographic characterization using X-ray Diffractometry (XRD), morphological characterization of crystal surfaces using Scanning Electron Microscopy (SEM), determination of tap density, determination of true density and solubility tests. All tests aim to determine and identify the physical characteristics of the isolated curcumin.

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Material and Method

Pycnometers (Iwaki), analytical balances (Ohaus), tap density testers (Jeol JSM 6510 LA), powder X-ray diffractometry (X'Pert-Pro MPD PW3040/60), zeta sizers (Horiba Scientific Nano Particle Analyzer, SZ-100), and differential scanning calorimeter DSC-60 Plus (Shimadzu, Japan) were the instruments used in this study.

Material

Curcumin, previously isolated from *Curcuma xanthorriza* at the Indonesian College of Pharmacy Bandung was used for this study. Aquadest, glycerin (P & G Chemicals), sorbitol (Cargill), PEG 400 (PETRONAS), propylene glycol (Dow Chemical Pacific), and 96% ethanol were utilised as test substances in this investigation.

Methods

Tap Density Determination

Curcumin (15 g) was placed in a 100 ml measuring cup and squeezed consistently on the Tap Density Tester. The tests were repeated thrice [17], and the percentage compressibility index was computed from equations 1 and 2.

$I = \frac{V_o - V_f}{V_o} \; x \; 100\%$ .....equation (1)

Rasio Hausner = $\frac{V_o}{V_f}$ .....equation (2)

Information:

I = Compressibility Index (%)

V_o = Volume of bulk

V_f = Compressed Volume

True Density Determination

An empty pycnometer was weighed, and 25 mL of the sample was placed in the pycnometer and dried with a tissue until no water dripped. The sample in the pycnometer was weighed and computed using mass density formulae (equation 3).

$\rho = \frac{m}{v}$ (3).

Where,

ρ = Sample density

m = Mass

v = Volume

Solubility Test

The solubility testing protocol utilized in this study adheres to the Pharmacopoeia RU (2015) guidelines by progressively increasing solubility. Solubility testing of curcumin was performed in the following solvents: propylene glycol, PEG 400, sorbitol, glycerin, and 96% ethanol.

The sample (50 mg) was stirred with 50 µL of solvent and observed for dissolution. The substance is said to be soluble if it is completely dissolved. If not completely soluble, a further 500 µL of solvent is added. If the substance completely dissolves, it is categorized as easily soluble. If not, another 1 mL of solvent is added. If it completely dissolves, then the substance is categorized as soluble. If the substance is not completely soluble, 3.5 mL of solvent is added. If the substance is completely dissolved, then the substance is categorized as rather difficult to dissolve. If the substance is not completely soluble, a dilution process is carried out by taking a sample solution of 1 mL and then adding 9 mL of solvent. If the substance completely dissolves, the substance is categorized as insoluble. If the substance does not dissolve completely, dilution is carried out again by taking a sample solution of 5 mL and then adding 45 mL of solvent. If the substance is completely dissolved, then it is categorized as very difficult to dissolve. If the substance is insoluble, then it is categorized as practically insoluble in this solvent.[18]

Determination of Zeta Potential

A zeta potential analyzer (Horiba Scientific Nano Particle Analyzer, SZ-100) was used to determine the potential zeta values of the isolated curcumin. The sample was placed in a vial, an aquadest was added, and sonicated for 15 minutes. After which, it was placed on a zeta sizer, and the electrodes were introduced. This experiment was repeated three times (triple) at the Research Center for Nano Science and Nano Technology at Bandung Institute.[19]

Morphological Characterization of Isolate Surfaces Using SEM

The samples were examined under the FMIPA ITB Laboratory's Scanning Electron Microscope (SEM) at magnifications of 1000x and 5000x. A test sample that will fit into the SEM chamber with some accommodation to prevent charge build-up was obtained and mounted rigidly on a specimen holder or stub using a conductive adhesive. The sample was placed in the SEM chamber, and air was evacuated to create a high vacuum. The electron beam was focused on the sample, and the surface was scanned to create an image. The different signals produced were collected using specialised detectors to obtain information about the surface's topography and composition.[20]

Characterization of Curcumin Isolate using XRD

The crystal properties of curcumin were determined in the angular range of 23° - 50°. A sample of the isolated curcumin was prepared for XRD analysis by grinding it into a fine powder and then loaded onto the XRD instrument. The settings of the equipment were adjusted to the appropriate parameters, followed by scanning. The sample X-ray diffraction patterns were collected and analysed to determine crystal structure.[21] XRD provides information regarding the sample's crystal structure, crystal size, and orientation.

Results and Discussion

Tap Density

The health benefits of curcumin have necessitated its increasing use as a pharmaceutical and cosmetic product. It is known to possess anti-inflammatory, anticancer, immuno-modulatory, hypolipidemic, and wound healing activities, etc. However, its formulation into a pharmaceutical product requires the characterization of its physical properties (solvent solubility, compressibility, surface area, etc.). Various physical parameters of curcumin isolated from *Curcuma xanthorriza* were examined in this study to provide valuable data to aid its formulation into a pharmaceutically stable and excellent product.

The compressible density test determines if curcumin can form a stable and compact mass when pressure is applied. The compressibility index can also predict the flow properties of the molecule. The compressibility value data of curcumin from the study was 16.463±0.517%. Based on the results of the compressibility experiment, the flow property of curcumin is categorized as quite good, with values ranging from 16 to 20%.[22] Compressibility is a measure of how well a material can be compressed without losing its properties. It is the ability of granules to form tablets with a certain amount of pressure. Compressibility is also usually called index carr's, which can be used to determine flow properties. The smaller compressibility values indicate that the granules will have good flow properties.[23] In the context of pharmaceutical tablet manufacturing, low compressibility of granules indicates that granules can be compressed into tablets without significant quality loss. This ensures that the tablet has consistent quality and retains its intended properties.[24] This compressibility value becomes significant during the process of its formulation into tablets, with the assurance of good flow qualities. It will aid in the formulation of good, compact, and uniform weights of tablets. Compressibility can also affect the process and quality of tablet formation because it can affect the flowability, hardness of tablets, fragility of tablets, and uniformity of tablets.[23]

True Density Test

True density is a term often used in the context of testing materials to determine the original or true density of a substance, expressed in grams per milliliter (g/mL). True density testing is used to determine a particle's density value without a compression technique. The lesser the particle porosity, the higher the sample density value. According to Table 2, the actual density test of curcumin yielded values of 1.116 ± 0.0086. These findings reveal that curcumin has a high enough density value to imply that the particles are firmly organized and have low

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porosity. The true density can affect the strength and density of tablets, the rate of dissolution and bioavailability, as well as the stability of the tablets. Tablets that are too dense can make tablet dissolution difficult, can inhibit absorption, and can cause physical and chemical damage.[25,23]

Solubility Test

The method of assessing the solubility of curcumin in various solvents was carried out in this study. This test aims to measure the level of solubility of curcumin in the solvent of choice. PEG 400, propylene glycol, sorbitol, and glycerin were the solvents employed in this investigation. These four solvents were utilized because they are often employed in the formulation of pharmaceutical dosage forms.

Table 3 indicates that curcumin has high solubility in PEG 400. PEG-400 is a polyethylene glycol with a low molecular weight. It is a colourless and highly hydrophilic liquid used in a variety of fields, including pharmaceuticals, food technology, and powder characterization. PEG 400 can boost a substance's solubility due to its stability and easily mixes with other components. In contrast, curcumin was insoluble in propylene glycol, sorbitol, glycerin, and ethanol. This may be due to its nonpolar nature, characterized by high carbon levels of its molecule. The more carbon in a compound, the more nonpolar the chemical will be. The solubility principle states that like dissolves like. Polar solvents will only dissolve polar substances.

Based on these findings, PEG 400 can be recommended for use in developing curcumin-based medicinal formulations. This solvent can be used for parenteral, topical, oral, ophthalmic, and rectal medicines in the pharmaceutical industry. It is commonly employed in preparations as ointment bases, plasticizers, suspending agents, emulsifiers, suppository bases, and lubricants in tablets and capsules.[26] Curcumin can be formulated into suspensions, emulsions, suppositories, and topical applications.

Table 1: Tap Density Test Results

Experiment	Compressibility Index (%)
1	17.037
2	16.176
3	16.176
Average	16.463
Standard Deviation	± 0.517

Table 2: True Density Test Results

Experiment	True density (g/mL)
1	1.121
2	1.106
3	1.121
Average	1.116
Standard Deviation	± 0.0086

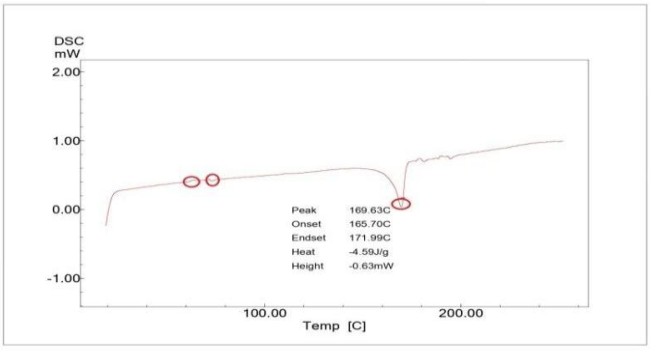
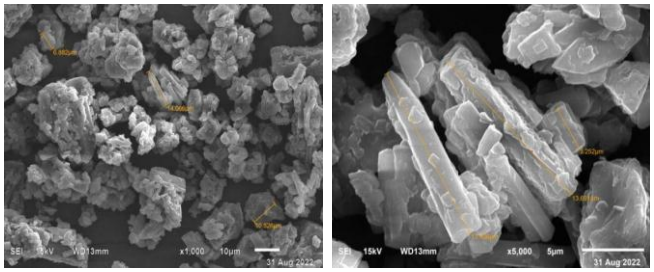


Figure 1: Curcumin Thermogram



a **b**

Figure 2: Curcumin Morphological Results a. 1000x magnification; b. 5000x magnification

Melting Point Determination using DSC

The melting point of curcumin was determined using the Differential Scanning Calorimetry (DSC) instrument. This test determines the temperature at which curcumin melts. The melting point is the temperature at which a solid becomes a liquid. The thermogram data in Figure 1 show the results of the melting point test of curcumin. Various peaks are shown in the thermogram (Figure 1), corresponding to the different phases of the melting process. The glass transition point is commonly defined as the first peak. The glass transition is the point at which a material's phase changes. The transition point of curcumin was observed in the thermogram at 60 °C. The crystallinity point that occurs at 75 °C is located at the top of both curves. This crystallinity point is frequently seen following the glass transition point. The melting point of curcumin is 169.63 °C at the top of the three curves. The high melting point of curcumin may have been due to intermolecular interactions. Compounds with solid intermolecular interactions typically have high melting points. This high melting point temperature suggests that curcumin is heat resistant. This finding can be utilized as reference data when selecting the best method for the development of curcumin-based products. A suitable temperature for processing products made from curcumin should be below the melting point range since temperatures above this range may lead to damage or decomposition.

Determination of the Potential Zeta Value

The potential zeta value of curcumin was evaluated to determine the stability of the dispersion storage system that has been formed. Because the potential zeta value can indicate the possibility of aggregation, it can be utilized as a reference to formulate suspensions. Table 4 shows the potential zeta test findings of curcumin. Curcumin has an average potential zeta value of -59.8 ± 0.608, which demonstrates that curcumin is stable since its potential zeta value is more than -30 mV or more significant than + 30 mV. It also means that its formulations could maintain good stability during storage with low chances of aggregation since the higher the potential zeta value, the greater the ability to prevent aggregation or the process of particle coalescing. The high zeta potential value of curcumin implies a strong repulsive attraction between the particles, with a low level of relative aggregation. Hence, a suspension product of curcumin may have good stability and a low risk of aggregation.

Results of Morphological Determination of Curcumin

Scanning Electron Microscope (SEM) was used for the determination of the particle size distribution and surface morphology of curcumin. This test was performed at two different magnification levels: 1000x to examine the particle size distribution and 5000x to examine the surface morphological shape. Figure 2 shows the images of the morphological analysis of curcumin.

According to Figure 2, the surface morphology of curcumin is roughly elongated like a beam with surface pores. Table 5 shows the particle size distribution predominantly in the 10m - 20m range, with a percentage of 51.51%. According to these findings, curcumin has a homogeneous or uniform particle size. Surface morphology and particle size distribution are interrelated and influence each other in determining the physical and chemical properties of a material. Surface morphology can affect the surface area of a material,

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while particle size distribution can affect the mechanical strength, chemical reactivity, and homogeneity of the material. Both of these factors can affect a material's ability to interact with the surrounding environment and can affect properties such as mechanical strength, chemical reactivity, and adsorption ability.[27]

Results of Determination of Crystal Properties

X-ray diffractometer (XRD) was used to determine the crystal characteristics of curcumin in this study. The results of measurements taken with this instrument are displayed as diffractogram graphs. Figure 3 depicts the diffractogram of the curcumin isolated from *Curcuma xanthorriza*.

The diffractogram of curcumin in Figure 3 indicates some peaks and noise. Peaks suggest a crystalline form in the curcumin sample, whereas noise indicates an amorphous nature of the compound.[28,29] The data in Appendix 7 show the steep peaks contained in the graph. The angles and intensities indicate a regular arrangement of atoms forming a crystalline plane whose number fluctuates at each apex. The various configurations of these atoms influence the intensity pattern. At an angle of 230-50°, curcumin exhibits an amorphous structure with a slight curvature and a wide pattern rather than crystallinity peaks. The Match was also used to examine the process of finding the crystal characteristics of curcumin. The Match Identification findings revealed that curcumin has a crystalline property of 42.09%.

Table 3: Solubility Test Results

Number of Parts	Volume (mL)	Solvent				
Solvent		**PEG 400**	**Propilenglikol**	**Sorbitol**	**Glycerin**	**Ethanol 96%**
< 1 part	< 50 µL	-	-	-	-	-
1 - 10	450 µL	Soluble	-	-	-	-
10 - 30	1 mL	Soluble	-	-	-	-
30 - 100	3,5 mL	Soluble	Soluble	-	-	-
100 - 1000	1 mL & 10 mL	Soluble	Soluble	-	-	Soluble
1000 - 10.000	5 mL & 45 mL	Soluble	Soluble	-	-	Soluble
Solubility Categories		Easily soluble	Moderately soluble	Practically insoluble	Practically insoluble	Slightly soluble

Table 4: Results of Potential Zeta Value Determination

Experiment	Zeta Potensial Value (mV)
1	-59.4
2	-59.5
3	-60.5
Average	59.8
Standard Deviation	± 0.608

Table 5: Curcumin Particle Size Distribution

Size Range	Number of Particles	Percent
3.0 – 10.0	23	34.85%
10.1 – 20.0	34	51.51%
20.1 – 30.0	7	10.60%
30.1 – 40.0	2	3.03%
	∑ =66	99.99%

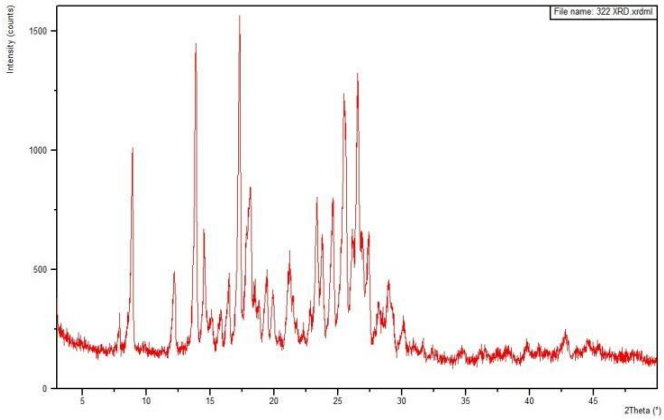

Figure 3: Diphratogram of Curcumin

Conclusion

The findings from this study showed that curcumin has crystalline characteristics with a long beam morphological shape, which confers better stability than other crystals and is more resistant to environmental and temperature changes. It has a fairly good flow rate to reduce the occurrence of aggregation and cohesion and, hence, increase the stability of its preparations. It is easily soluble in PEG 400 (used in various applications, including in the manufacture of pharmaceutical preparations and cosmetics), and preparations that are easily soluble in PEG 400 are more stable and have a long shelf life. The study also revealed that curcumin has a good potential zeta value, reduced tendency of agglomeration, and increased stability and durability of its preparations. This property also leads to more homogeneous and well-dispersed particle formulations, improving product effectiveness and safety. The results of this study could serve as a database for the formulation of stable and effective curcumin-based pharmaceutical products.

Conflict of Interest

The authors declare no conflict of interest.

Authors' Declaration

The authors hereby declare that the work presented in this article is original and that any liability for claims relating to the content of this article will be borne by them.

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