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Ultrasound-Assisted-Extraction (UAE) of Phenolic Compounds from Bamboo Shoot and Its Potential Source of Anti-Inflammatory Agents for Gout Treatment

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Abstract: The gouty arthritis is caused by the deposition of monosodium urates (MSU) crystals in joints and characterized by hyperuricemia, a long-lasting abnormally high concentration of uric acids in the blood. Existing medications for gout arthritis such as NSAIDs and Allopurinol are not always effective and may have side effects to the patients. Therefore, there has been increasing interest in looking for better medications to control gout, especially on compounds that can inhibit xanthine oxidase and cyclooxygenase. As such, green inhibitors from plants are widely investigated. This study utilized bamboo shoot as the source for green inhibitors. Soxhlet with UAE was employed for extraction and using different solvents, namely; water, methanol and water: methanol with varied sonication times which are 15 minutes, 30 minutes, and 45 minutes, thus different yields of extract were collected. The capacity of the extracts to inhibit XO activity was assessed through XO assays with Allopurinol as the positive control. Then, the potential phenolic substances that may contribute to the effects were identified with HPLC. The results showed that the concentration of water-methanol extract with 30 minutes of sonication is 73.00 % higher concentration compared to without sonication and 71.00 % higher concentration than water-only extract. This could be due to water only allowing the extraction of polar components, hence lower content of extract. In agreement, the same method also displayed the highest value of XO inhibition (74.15 %) which means it has better anti-inflammatory effect compared to other extracts. When comparison was made between the water-methanol extract and Allopurinol, the difference was only 20.00 % in inhibiting XO activity. Sonication indeed enhances the extraction process where 30 minutes of sonication gives the optimum time for the extraction of anti-inflammatory compounds from bamboo shoots. In addition, the extracts may contain other anti-inflammatory components but ferulic acid and ellagic acid, as they were not detected by HPLC. The phenolic groups which contribute to anti-inflammatory activities are present in the bamboo shoots. It is hopeful that this study can provide preliminary data on the potential use of bamboo shoots as an anti-inflammatory source.

Keywords: Gout, Anti-inflammation, XOI, Allopurinol, Phenolic compound

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1. Introduction

Gout is a common form of inflammatory arthritis that is very painful. It usually affects one joint at a time which often the big toe joint [1]. There are times when symptoms get worse, known as flares, and times when there are no symptoms, known as remission. Repeated bouts of gout can lead to gouty arthritis, a worsening form of arthritis. Gout occurs when urate crystals accumulate in joint, causing the inflammation and intense pain of a gout attack by xanthine oxidase [2]. Urate crystals can form when having high levels of uric acid in your blood [3]. Body produces uric acid when it breaks down purines — substances that are found naturally in your body. Purines are also found in certain foods, including red meat and organ meats, such as liver [4]. Purine-rich seafood includes anchovies, sardines, mussels, scallops, trout and tuna [5]. Alcoholic beverages, especially beer, and drinks sweetened with fruit sugar (fructose) promote higher levels of uric acid [6]. Normally, uric acid dissolves in blood and passes through kidneys into urine [7]. But sometimes either body produces too much uric acid or kidneys excrete too little uric acid. When this happens, uric acid can build up, forming sharp, needle-like urate crystals in a joint or surrounding tissue that cause pain, inflammation and swelling. There are few factors that lead to gout which are genders and sex that commonly occurs in men as women tend to have lower uric acid levels, family history of gout, recent surgery or trauma and many more [8]. The sign and symptoms of gout always occurs suddenly, and often at night. They also include intense of joint pain, lingering discomfort, inflammation and redness, and limited range of motion [9]. Inflammation which is one of symptoms of gouty arthritis caused by the deposition of monosodium urates (MSU) crystals in joint and characterized by hyperuricemia, a long-lasting abnormally high concentration of uric acids in the blood [10]. This process generates oxygen metabolites, which damage tissue, resulting in the release of lysosomal enzymes that induce an inflammatory response.

Existing medications for gout arthritis such as NSAIDs and Allopurinol are not always effective due side effects and poor compliance [11]. Therefore, continuous search for more natural-based medications for gout is warranted. Bamboo shoot has been reported to possess anti-inflammatory effect. However, studies on bamboo shoots, which could have potential green inhibitors are limited. The extracts of bamboo have been reported to meet as anti-inflammatory, anthelmenthic, antibacterial, diuretic property, antiulcer, antifertility, antimicrobial and hypoglycaemic activities [12]. In this case, bamboo shoot has high phenolic content in which is one of it is ferulic acid may reduce the inflammatory activity [13]. In this study, the extract potential anti-inflammatory substances were extracted from bamboo shoot by using Soxhlet extraction and ultrasound assisted Soxhlet extraction (UAE) method at different parameters, to assess the capacity of extracts in reducing inflammation through xanthine oxidase inhibition and to identify potential substances that may be involved in anti-inflammation through HPLC.

2. Materials and Methods

First, extraction of the bamboo shoots by using the Ultrasonic Assisted Extraction (UAE) in which the ultrasound in the solvent producing cavitation accelerates the dissolution and diffusion of the solute as well as the heat transfer, which improves the extraction efficiency [14]. After the extraction method, by using the xanthine oxide assays, the sample extracts were assessed in inhibiting inflammatory activity. Lastly, the identification of phenolic compound through HPLC-PDA was conducted.

2.1 Materials

Bamboo shoots (*Gigantochloa albocillata* sp.), Methanol, Allopurinol, xanthine, xanthine oxidase (bovinemilk), ferulic acid standard and ellagic acid standard were purchased from Sigma-Aldrich Chemicals. Hydrochloric acid (HCl), acetonitrile and acetic acid of analytical grade were obtained from Merck. Potassium phosphate buffer (pH 7.4) were purchased from Sigma-Aldrich Chemicals.

2.2 Preparation of plant material

Bamboo shoot shells from 15 kg *Gigantochloa albocillata* bamboo shoots was separated and air-dried at 30 °C. The shoots were cut into cubes about 3 cm each side and dried for two days at 110 °C using drying oven [15]. Prior to the extraction process, the dried bamboo shoots were grinded through a grinder and kept dry in a jar [16].

2.3 Extraction of bamboo shoot

Three different solvents which are 100.00 % distilled water, 100.00 % methanol and 50.00 % distilled water: 50.00 % methanol were prepared in 250 ml distillation flask. 10 gram of dried powdered bamboo shoots were added in each teabag for the Soxhlet extraction for 5 hours. Six samples were collected after the extraction process. UAE was performed with a fixed-frequency (40 kHz) ultrasonic bath. In conical flasks, six samples that collected of 50 ml each were sonicated in the ultrasonic bath for varied times which are 15 minutes, 30 minutes and 45 minutes [17]. Each extract was evaporated at 40 °C using a rotary evaporator. Then, the concentrations of extracts were spectrophotometrically conducted at 760 nm in this process to determine the concentration based on gallic acid standard curve [18].

2.4 Xanthine Oxide inhibitory activity

The samples were subjected to an XO inhibitory activity assay measured spectrophotometrically at 295 nm in this process to determine the XOI activity [19]. Allopurinol, a well-known XOI, was used as a positive control for the inhibition test at different concentrations; 10 µg/ml, 25 µg/ml, 50 µg/ml and 100 µg/ml [20]. The reaction mixture included 300 µl of 50 mM phosphate buffer (pH 7.4), 100 µl of sample solution dissolved in distilled water, 100 µl of freshly made enzyme solution (0.2 units/ml xanthine oxidase in phosphate buffer), and 100 µl of distilled water. The assay mixture was pre-incubated for half an hour at 37 °C. Then, into the mixture, add 200 µl of substrate solution (0.15 mM xanthine) [21]. The mixture was re-incubated for 30 minutes at 37 °C. The reaction is then stopped by adding 200 µl of 0.5M hydrochloric acid, HCl. Measure the absorbance with a UV/VIS spectrophotometer against a blank prepared in the same manner but with the phosphate buffer in replacing of the enzyme solution. To maximise uric acid formation, prepare another reaction mixture (control) with 100 µl of distilled water instead of test compounds. By employing the equation stated below to assess the degree of XO inhibitory activity [22]. Thus, use Eq. 1 [23] to calculate XOI activity, where is the activity of XO without test extract and is the activity of XO with test extract.

$$\%\ XO\ inhibition = (1 - \frac{\beta}{\alpha}) \times 100\ Eq.\ 1$$

2.5 Detection of potential compounds by HPLC

HPLC profiles of bamboo shoot extracts were determined. Analysis of all samples was performed using a HPLC Waters 2695 Alliance (Waters®, Milford, MA, USA) combined with a PDA Waters 2998 (Waters®, Milford, MA, USA). HPLC system was equipped with a column compartment with temperature control, on line degasser, quaternary pump, auto sampler and auto injector. The analyses were realized using a reverse phase C18 chromatograph column (Vertical®, Bangkok, Thailand) with 5 µm particle size, 4.6 mm internal diameter and 50 mm length with injection volume 10ml, total flow 0.2 ml/min, column oven temperature 25 °C and detection wavelength 320 nm. 300 µl of bamboo shoot extracts were dissolved in 3 ml of ultrafiltration pure water for the analysis where the peak detected for extracts were compared to the peak detected for standards; ferulic acid and ellagic acid [24].

3. Results and Discussion

3.1 Effect of ultrasonication and different solvents in extracting anti-inflammatory related compound.

Experiment has been carried out by using two different methods; Soxhlet extraction only and Soxhlet with Ultrasound Assisted Extraction (UAE) with three different solvents; 100.00 % distilled

water, 100.00 % methanol and 50.00 % distilled water: 50.00 % methanol, and different sonication time; 15 minutes, 30 minutes and 45 minutes. The effect of different techniques and parameters on concentration of total phenolic content was evaluated through Gallic acid standard calibration curve. Methanol 100.00 % is a good solvent to extract organic solvent to extract most of the compounds, but it is not that polar compared to water. So, combination of methanol-water will be the best solvent as is it able to extract most of the compounds from polar-non polar [25].

Figure 1 illustrates the concentration of anti-inflammation agent of bamboo shoot extracts using different solvent such as water, methanol and water-methanol has been carried out. In this study only used the methanol and distilled water where methanol is a good solvent for extraction but it is not polar enough as compared to water. However, the mixture between water and methanol helps to extract efficiently most of polar-non polar compounds [26]. Other than that, the ultrasonication increases the efficiency of the extraction process as it helps to breakdown the compound much better than the extract obtained through Soxhlet extraction only. Hence, the extraction yields increased.

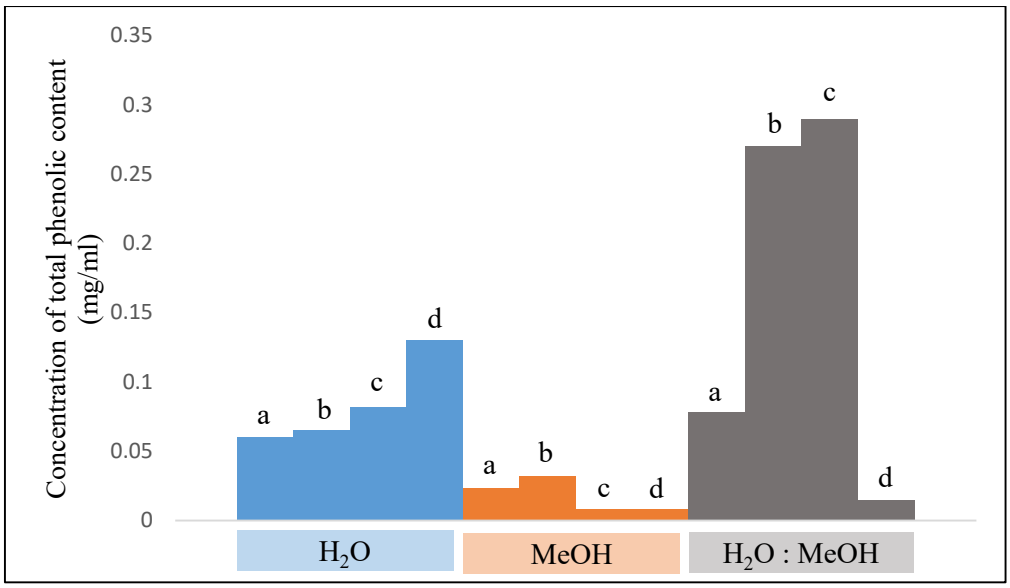

Figure 1: The concentration of total phenolic content successfully extracted using three different extracting solvents; water, methanol and water-methanol by a) non-sonicated b)15 minutes of sonication c) 30 minutes of sonication and d) 45 minutes of sonication

The results showed that the concentration of water-methanol extract with 30 minutes of sonication is 73.00 % higher concentration compared to without sonication and 71.00 % higher concentration than water-only extract. This could be due to water only allowing the extraction of polar components, hence lower content of extract.

3.2 Determination of Xanthine Oxidase Inhibition Activity.

Xanthine oxidase assays has been carried out to evaluate the Xanthine Oxidase activity of the bamboo shoot extract. The evaluation of XO inhibitory activity of different method; Soxhlet alone, Soxhlet assisted ultrasonic using three different solvents; water, methanol and water-methanol with 15, 30 and 45 minutes each solvent were conducted at a concentration of 100 µg/ml, at which some of the extracts found to have XO inhibitory activity.

Table 1 shows the percentage of xanthine oxidase inhibition at different concentrations of allopurinol as positive control which are 10 µg/ml, 25 µg/ml, 50 µg/ml and 100 µg/ml. The results were increasing when the concentrations increased, and the highest value achieved for Allopurinol is 93.69 %. the results then were compared with the extracts to measure the anti-inflammatory inhibition through Xanthine Oxidase assays activity as shown in Table 2.

Table 1: Xanthine oxidase Inhibition (%) of Allopurinol at different concentrations; 10 µg/ml, 25 µg/ml, 50 µg/ml and 100 µg/ml

Concentration (µg/mL)	XOI (%)
10	56.32
25	65.12
50	83.34
100	93.69

In agreement with high phenolic compounds extracted with ultrasonication, XOI activity also shows similar trend. As seen in Table 2, the extracts from Soxhlet extraction with UAE for 30 minutes obtained the highest capacity of XOI which is 74.15 % inhibition of XOI. Meanwhile, the positive control, Allopurinol recorded 93.69 % inhibition of XO activities at a relatively similar concentration. When comparison was made between the water-methanol extract and Allopurinol, the difference was only 20.00 % in inhibiting XO activity, indicating its potential to be used for gout treatment. Some of data from extracts such as for extraction using 100.00 % methanol and 45 minutes of time sonication using water-methanol solvent are not available because of the concentration is too low. According to previous study, the changes of xanthine oxidase inhibition (%) in canned bamboo shoots show a significant effect as they increase from 20.00 % up to 60.00 % by time (10, 20, 30, 40 minutes) and heating temperature for 30 ℃, 80 ℃ and 95 ℃ [27]. This shows that time and temperature are other important factors instead of the types of solvents to be considered when conducting the XOI activity.

Table 2: Xanthine Oxidase Inhibition (%) of bamboo shoot extract for Soxhlet alone and Soxhlet with ultrasonication assisted extraction method

Method	Solvent	Xanthine oxidase Inhibition (%)		
Soxhlet	H_2O	16.67		
	MeOH	N/A		
	H_2O: MeOH	17.68		
		Sonication Time (min)		
		15	30	45
Soxhlet + Ultrasound	H_2O	16.33	31.14	56.36
	MeOH	N/A	N/A	N/A
	H_2O: MeOH	72.05	74.15	N/A

The higher the concentration of the extract, the higher the percentage of XOI activity. This could be due to the increasing presence of phenolic compounds in the extracts. A strong inhibition activity of XO exhibited by allopurinol proved its effective usage on the clinical treatment of gout [28]. In parallel with the highest yield of extracted phenolic compounds seen, the same extract which is the extracts by Soxhlet assisted with 30 minutes ultrasonication using 50.00 % distilled water: 50.00 % methanol as extracting solvent showed highest capacity of XOI activity. It is interesting to investigate what type of phenolic compounds that may contribute to this beneficial effect.

3.3 Identification of potential phenolic compounds.

Studies on bamboo shoots have been carried out in providing alternative bioactive components where they have anti-inflammatory agents in management of various diseases including gout arthritis. Phenolic compounds are one of the most beneficial groups used for inhibiting the inflammation and reducing the xanthine oxidase activity among other bioactive compound in the bamboo shoots [29] In this study, identification of potential phenolic compound such as ellagic acid and ferulic acid was done using HPLC-PDA.

HPLC analysis for standard of ellagic acid was prepared using six standard solutions; 10; 30; 50; 60; 80 and 100 µg/mL. Based on Figure 2, ellagic acid was detected in round 3.9 minutes, the highest peak indicated in a short time.

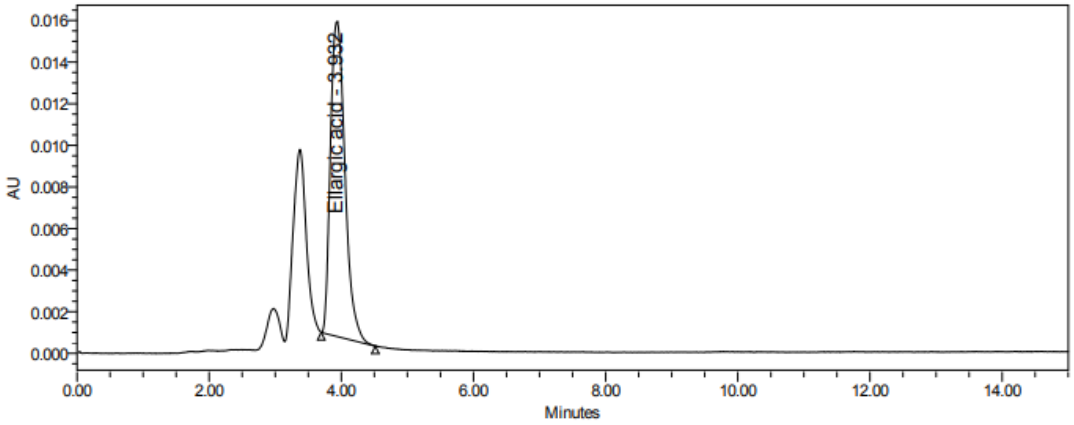

Figure 2: The retention time for Ellagic acid as standard using HPLC at 100 µg/mL

Figure 3 illustrates the comparison to the bamboo shoots extracts where the targeted compound is being detected in range of 4.1 – 4.2 minutes which is out of the range detected for the ellagic acid. This concerns may related to the pre-treatment method which the concentration is too low; 1/10 dilution factor. The detector cannot read as much as they can so that the peak is out of the range and obtain a small number of analyses. According to previous study, the ellagic acid was detected at 22.54 minutes using HPLC-DAD on an Intertsil ODS-3 reverse phase C18 column (5 µm, 250 mm×4.6 mm i.d) thermostatted at 40 °C. The solvent flow rate was 1.5 mL/min. The sample volume injection was 20 µL. The mobile phases used were: (A) 0.50 % acetic acid in water, (B) 0.50 % acetic acid in methanol [30]. This may occur because of the shorter time detected for highest peak due to lower concentration of extracts.

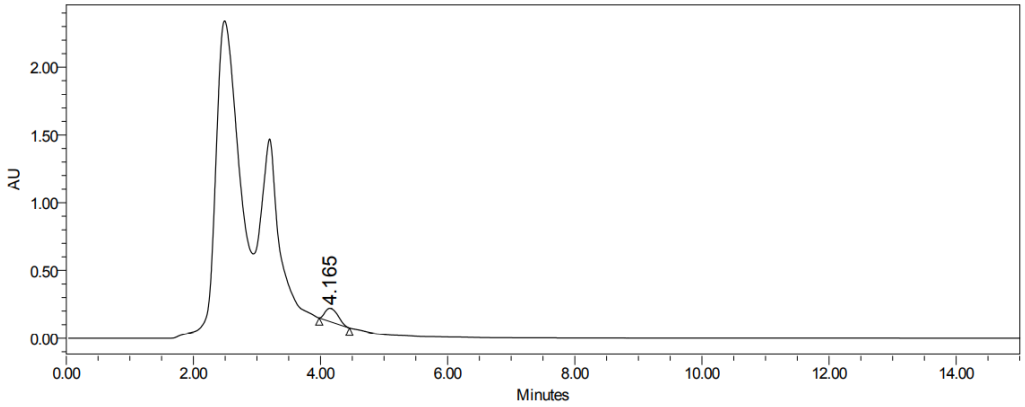

Figure 3: Chromatograph of extract for identification of ellagic acid at 100 µg/mL

Similar to ellagic acid, HPLC analysis for standard of ferulic acid was also prepared using six standard solutions; 10; 30; 50; 60; 80 and 100 µg/mL. Based on Figure 4, ferulic acid was detected in round 4 minutes, the highest peak indicated in a short time.

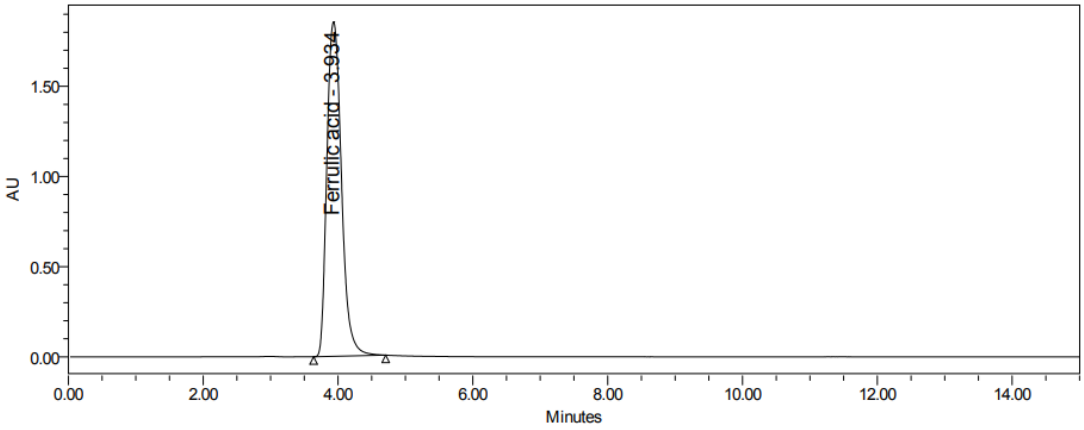

Figure 4: The retention time for Ferulic acid as standard using HPLC at 100 µg/mL

Figure 5 illustrates the chromatograph of extracts where the targeted compound is being detected in range of 4.1 – 4.2 minutes which is out of the range detected for the ferulic acid. This concerns may related to unknown phenolic compound other than ferulic acid and ellagic acid since only two of standard that have been carried out through HPLC analysis.

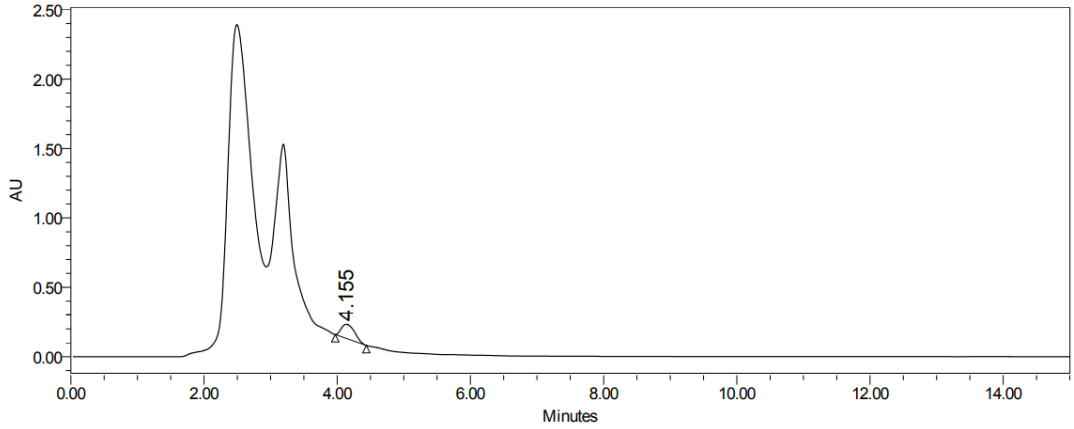

Figure 5: Chromatograph of extract for identification of ferulic acid at 100 µg/mL

Previous study presented using the same method with this study, ferulic acid was detected at 4.5 minutes [31]. The absorbance units (AU) detected for the extracts is 0.2 compared to the standard of ferulic acid which is 1.8. None of the extracts detected the presence of ferulic acid and ellagic acid compound based on the chromatography. This is because the peak is too low and cannot be seen in short period of time. The results have shown that there are other phenolic compounds that may be present in bamboo shoots extract instead of ferulic acid and ellagic acid with further studies.

4. Conclusion

Inflammation is major factors that lead to gout arthritis. The origin of MSU crystals inflammation is complex. Synovium MSU crystals are enveloped in neutrophils/monocytes, when reactive oxygen species (ROS) generation and cell death are initiated [32]. Many studies on the established drugs such as Allopurinol and NSAIDs has been carried in order to find an alternative way in managing the disease itself [33]. Medicinal plant such as bamboo shoots contain bioactive compound such as flavonoids and others phenolic compounds [34]. In this study, two methods of extractions with three different extracting solvents were used to assess which method would give the best extract to inhibit XO activity. It was found that the concentration of phenolic compounds in the bamboo shoot extracts is increasing by time when using extraction assisted by UAE. 30 minutes of sonication time by using water-methanol solvent is the best extraction method. In agreement, XOI activity in the same extract resulted the highest

the XOI (%), the best method to extract anti-inflammation substances. Lastly, the results for have shown that there are other phenolic compounds that are present in bamboo shoots extract instead of ferulic acid and ellagic acid and therefore require further study to identify the other potential source of anti-inflammatory activity from bamboo shoot for gout treatment.

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