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# Recovery of Anti-Cancer Damnacanthal from Roots of *Morinda citrifolia* by Microwave-Assisted Extraction

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# Recovery of Anti-Cancer Damnacanthal from Roots of *Morinda citrifolia* by Microwave-Assisted Extraction

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**Abstract:** This study investigated the effects of material particle size, irradiation time, extraction temperature, type of solvents, ethanol composition, and the ratio of liquid-to-sample on microwave-assisted extraction (MAE) of roots of *Morinda citrifolia* to obtain the most important anti-cancer compound, *damnacanthal*. The highest recovery of the compound was obtained after 5 min of MAE of small particle size material at 100 and 120°C. Longer extraction time caused the decrease in percent recovery due to the decomposition of the compound. Among the pure solvents tested, acetone and methanol gave the highest recovery. However, the use of ethanol-water solution (80% v/v) could considerably improve the yield of damnacanthal extracted. MAE was found to give the highest extraction efficiency when compared with other extraction methods such as extraction with electrical heating, soxhlet extraction, and ultrasound-assisted extraction (UAE).

**Keywords:** Anti-cancer, damnacanthal, MAE, *Morinda citrifolia*, UAE

## INTRODUCTION

*Morinda citrifolia* (Noni or Yor) is one of the most well-known tropical plants which contains several bioactive compounds, responsible

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for maintaining overall health and treating various diseases (1). The most important group of the therapeutic components in this plant is anthraquinones, which has been shown to process various properties including anti-bacterial, anti-viral, and anti-cancer activities (2). Antraquinones are usually found in the roots of noni, and the most medicinally active and the most valuable compound in this group is the cancer-inhibiting agent called *damnacanthal* (3).

Usually, plant metabolites are present in a small amount in a specific part of the plant. Therefore suitable extraction techniques are required to most effectively remove these high-value compounds from their source. The investigation of new extraction processes including ultrasound-assisted extraction (UAE), microwave-assisted extraction (MAE), and subcritical water extraction (SWE) has become an active research area (4–7). In our previous studies, we have investigated various methods for the extraction of total anthraquinones from *M. citrifolia* roots which included SWE (6–7), UAE (8), and MAE (9). Of these methods, MAE has high potential as it could be used to effectively reduce the amount of solvent used without lowering the antioxidant activity of the extract (9). Several other recent studies have also applied MAE for extraction of various plants such as caraway seeds (10), green tea leaves (11), *Nothapodytes foetida* (12), and *Ganoderma atrum* (13). The process was also applied together with ultrasound for the extraction of isoflavonoids from pueraria (5). These studies reported that the enhanced extraction efficiency by MAE was due to the ability of the transmitted microwave to simultaneously and homogeneously penetrate the plant materials and interact with polar molecules such as water, which could then cause rapid heating within the whole plant matrix (14).

Hemwimol et al. (9) reported the suitable conditions for MAE of total anthraquinones. Unfortunately, the results on the suitable conditions for extraction of the specific *damancanthal* compound could be entirely different, and thus could not be inferred from this previous study (15). It is therefore the aim of this study to develop a suitable process for MAE of *damnacanthal* from *M. citrifolia.* Here, the effects of various MAE parameters on extraction efficiency such as sample particle size, time, temperature, types of solvents, solvent compositions, and solvents-to-sample ratio were investigated. The results were also compared with those obtained by other methods such as extraction with electrical heating, UAE, and soxhlet extraction.

# EXPERIMENTAL

## Plant Material and Chemicals

The fresh root of *M. citriforia* was harvested, washed, and dried in an oven at about 50°C for 2 days. The dried root was then ground to obtain the sample of two particles sizes: 0.25 mm using a mortar and a pestle and 0.02 mm using a ball mill (Planetary Ball Mill PM100, Retsch GmbH & CO.Kg., Germany). Solvents used in this study were acetonitrile (99.9%, HPLC grade), methanol (99.9%, HPLC grade), ethanol (99.9%, analytical grade), and acetone (99.5%, HPLC grade), and were purchased from VWR International Ltd, UK.

## MAE

A MARS 5 (1200 W, 2450 MHz) microwave accelerated system from CEM Corp. (Mathews, NC, USA) was employed for MAE. The unit was equipped with twelve 100 ml closed PEEK vessels (only three were used for the experiment) covered with special TFM sleeves, a power sensor, a pressure sensor, a temperature sensor, and a temperature controller. The schematic diagram of the apparatus is shown in Fig. 1.

Into each of the three MARS 5 vessels, 0.1 g of ground dried roots was added with a specified amount of a solvent. The vessels

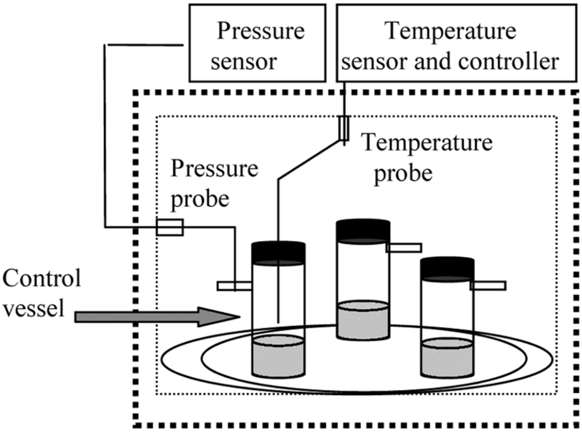

*Figure 1.* Schematic diagram of MAE system.

were placed symmetrically into the microwave system. As shown in Fig. 1, a pressure sensor, a temperature sensor, and a temperature controller were attached to one of the vessels, in which the system pressure was measured and the system temperature was controlled. For all experiments, 60% of power output (60% of 1200 W) was used and the ramping time for all extraction runs was 2 min. Extraction variables for MAE efficiency included extraction time (5, 10, 15, 20, and 30 min), extraction temperature (60, 80, 100, and 120°C), type of solvent (acetonitrile, methanol, ethanol, and acetone), composition of solvent (ethanol:water of 20%, 50%, and 80%), and solvent-to-sample or volume of extraction solvent/weight of the root sample (50, 80, 100, and 150 ml/g). After irradiation, the vessels were allowed to cool for 5 min and the solution was filtered through a filter paper (Whatman, no. 1, 125 dia.) in order to separate it from the sample residue.

## Extraction with Electrical Heating

For extraction of *M. citrifolia* root with electrical heating, the root sample was extracted with 8 ml of 99.9% (v/v) ethanol and 80% ethanol in water at 120°C for 30 min in a 8.8 ml closed batch pressure vessel (SUS-316 stainless steel, AKICO, Japan), placed in an electrical furnace, where heating was provided from the outer surface of the pressure vessel. When the furnace temperature reached a set temperature of 120°C, the extractor charged with the sample and extraction solvent was placed in the furnace. At this point, the extraction time started. It is noted that approximately 5 min was required for the actual extraction temperature (measured by another thermocouple inserted at the center of the extractor) to reach the set furnace temperature. After extraction was complete, the vessel was allowed to cool for 5 min and the solution was filtered through a filter paper (Whatman, no. 1, 125 dia.) in order to separate it from the sample residue.

## Soxhlet Extraction

In Soxhlet extraction, the root sample was placed into a cellulose extraction thimble (Whatman, England) and was extracted with ethanol with the approximate cycle of 7 cycles $h^{-1}$, until the solvent was clear or approximately 4 h.

## UAE

UAE was carried out in an ultrasonic bath, 275DAE (Crest Ultrasonics, USA) having the frequency of 38.5 kHz and the power rating of 270 W. The system consisted of a rectangular container (23.5 cm × 13.3 cm × 10.2 cm) containing 2.2 L of water, and to which two 38.5 kHz transducers were annealed at the bottom. In a 28 ml glass tube, 0.1 g of the root sample was extracted with 10 ml of solvent (99.9% ethanol or 80% ethanol in water). The tube was then partially immersed into the ultrasonic bath, such that the bottom of the flask was approximately 5 cm above the bottom of the bath and the solvent surface in the flask was kept at the level of the water in the ultrasonic bath. Extraction was carried out at the power setting of 3 which was measured to be 15.7 W with a wattmeter energy check 3000 (Voltcraft, Germany) and at the temperature of 60°C for up to 60 min.

## RP-HPLC Analysis of Damnacanthal

The content of damnacanthal in all extracts was analyzed using reversed phase high performance liquid chromatographic (RP-HPLC) equipped with a high pressure pump (Prostar 240, Varian, USA) and a photodiode array detector (Prostar 335, Varian, USA). The percent recovery of damnacanthal was then determined from the ratio of the amount of damnacanthal extracted to the total amount (100%) in the root sample, which was determined by the extraction of the roots 3 times with MAE at 120°C for 5 min. For the preparation of the sample for RP-HPLC analysis, the extracts were concentrated using a vacuum evaporator, and redissolved in 5 ml of acetonitrile. The clear solution was removed and the residue was then dissolved in about 10 ml of DMSO. Both acetonitrile and DMSO fractions were filtered through a membrane filter (0.45 µm, Millipore, USA) before being subjected to HPLC analysis following the method modified from Zhang et al. (16). The analysis was carried out at room temperature using a Phenomenex Luna C18, 100 A pore size, 5 µm particle size, 250 mm × 4.60 mm I.D. column. The mobile phase consisted of a mixture of 0.05% phosphoric acid aqueous solution (A) and acetonitrile (B) and the following solvent gradient was applied: 0–20 min, 20–28% A, 80–72% B; 20–30 min, 28–45% A, 72–55% B; 30–55 min, 45–10% A, 55–90% B. The flow rate of the mobile phase was 1 ml/min and an injection volume was 50 µL and the UV detection wavelength was 250 nm. A standard calibration curve was made from a plot of peak areas versus concentrations for a series of standard solutions.

## RESULTS AND DISCUSSION

### MAE

#### Effect of Materials Size

The material size and distribution usually have a significant influence on the performance of MAE. In the study, the experiment was carried out to determine the percent recovery for samples of two different particle sizes (0.25 and 0.02 mm). The microwave extraction was carried out at 60°C in which 0.1 g of root sample was extracted with 10 ml of 99.9% ethanol for various durations of 5, 10, 15, 20, 30, and 60 minutes, including ramping time and holding time. The results in Fig. 2 show the increase in the percent damnacanthal recovery as the extraction time increased for both sizes of the root material. However, the percent recovery was found to be significantly higher for the small particle size material (17). In the small size sample, the mass transfer limitation was reduced as the larger overall surface area of the small sample allowed better contact between the root sample and the solvent. The small sample was therefore used in the subsequent experiments.

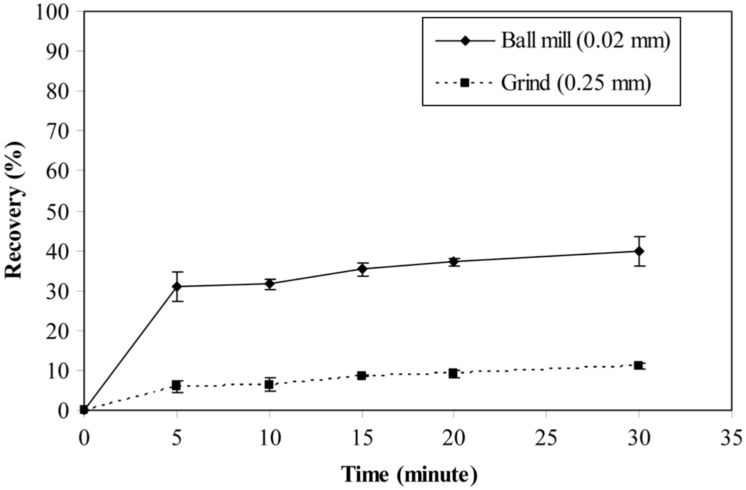

***Figure 2.*** Effect of materials size on percent recovery of damnacanthal from MAE, extraction temperature: 60°C, solvent-to-sample ratio: 100 (10 ml of 99.9% ethanol/0.1 g of sample).

## Effect of Irradiation Time and Temperature

Experiments were conducted to determine the effects of MAE time from 3 to 30 minutes and temperature from 60 to 120°C on percent recovery of damnacanthal. The sample-to-solvent ratio was 0.1 g of roots sample to 10 ml of 99.9% ethanol. The results in Fig. 3 show that at lower extraction temperatures of 60 and 80°C, the percent recovery of damnacanthal increased when the irradiation time increased from 5 to 30 minute. The percent recovery of damancanthal at 60°C and 80°C were comparable with the latter being slightly lower than that obtained, possibly due to the decomposition of the compound at high temperature. At higher temperatures of 100 and 120°C, the percent recoveries increased as the irradiation time increased up to 5 minutes, at which the percent recoveries of 33.29 and 44.25 were obtained for extraction at 100°C and 120°C, respectively. These results were obtained after only 3 to 5 min irradiation time.

The higher recoveries at higher MAE temperatures could be attributed to the increase in the solubility of the compound, caused by the increase in the molecular motion of the compounds at elevated temperature. Moreover, at high temperature, the solvent density and viscosity decreased, resulting in increased mass transfer of the solvent into the matrix of plant (9,13,17). However, as can be seen from Fig. 3, when the irrdiation time further increased, the pronounced decrease in the

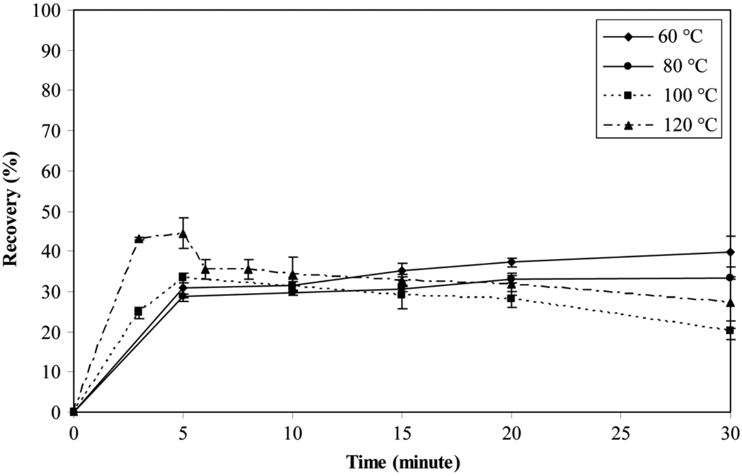

*Figure 3.* Effect of extraction temperature on MAE efficiency of damnacanthal, material size 0.02 mm, solvent-to-sample ratio: 100 (10 ml of 99.9% ethanol/0.1 g of sample).

extraction efficiency was observed, indicating that damnacanthal decomposed.

## Effect of Solvent Type

In MAE, the most suitable solvent should be selected based on the capacity of the extraction solvent for absorbing and transmitting the microwave energy. In addition, the solvent should be able to dissolve the target analytes or, in other words, the polarity of the extraction solvent should match that of the target compound. In this study, the effect of the solvent type on the percent recovery of damnacanthal was determined. The root material was extracted with organic solvent using MAE at 120°C for 3 min and with the solvent-to-sample ratio of 100 (10 ml of 99.9% ethanol to 0.1 g of sample). Figure 4 shows the percent recovery of damnacanthal obtained by various extraction solvents (acetone, methanol, ethanol, and acetonitrile).

In general, the ability of the solvent under microwave field to absorb and transmit the microwave energy would be determined by the two parameters defining the dielectric properties of the solvent. These are the dielectric constant ($\varepsilon'$) and dielectric loss ($\varepsilon''$), whose ratio (dielectric loss to dielectric constant) defines the dissipation factor ($\delta$). The solvent that heats up rapidly under microwave extraction usually has a high

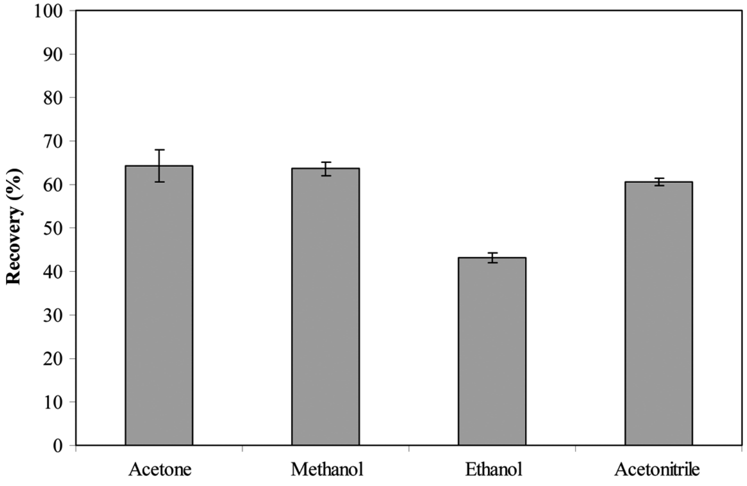

***Figure 4.*** Effect of solvent type on MAE efficiency of damnacanthal, material size: 0.02 mm, extraction temperature: 120°C, extraction time: 3 min, solvent-to-sample ratio: 100.

**Table 1.** Dielectric constant and dissipation factor of solvents

| Type of solvents | Polarity index | Dielectric constant $\varepsilon'^{a}$ (F/m) | Dielectric loss $\varepsilon''^{b}$ | Dissipation factor $\delta^{b}$ |
|---|---|---|---|---|
| Acetone | 5.1 | 20.7 | 11.5 | 0.5555 |
| Methanol | 5.1 | 32.7 | 15.2 | 0.6400 |
| Ethanol | 5.2 | 24.3 | 6.1 | 0.2286 |
| Acetonitrile | 5.8 | 37.5 | 2.3 | 0.062 |
| Water | 9 | 80 | 12 | 0.15 |

[a] Determined at 20°C.
[b] At 2450 MHz.

dielectric constant and dielectric loss. The values for dielectric constants and dissipation factor are listed in Table 1 (18). Of the solvents tested in this study, acetone and methanol were found to give the highest recovery. As the two solvents have the highest values of dielectric and dielectric loss constants, they quickly absorb much of the microwave energy and transform it into heat. Acetonitrile and ethanol have higher dielectric constants but much lower dissipation factors compared with acetone and methanol. Therefore the microwave heating rates should be lower than those of the other two solvents. The extraction results however showed that ethanol gave the lowest extraction efficiency while acetonitrile gave rather high efficiency despite the very low value of dissipation factor. The high efficiency of MAE with acetonitrile could be a result of its polarity (dielectric constant) which is slightly higher than that for ethanol, and which could be more suitable for solubilization of a slightly polar compound such as damnacanthal.

Although acetone, methanol, and acetonitrile gave a higher extraction efficiency than ethanol, ethanol is more widely acceptable as it complies with good manufacturing practice. In this study, ethanol was therefore chosen as an appropriate extraction solvent. However, the efficiency of extraction could be improved by adjusting the polarity by the addition of water and thus, in the subsequent experiment, the effect of ethanol composition in the ethanol water mixture on the extraction efficiency was investigated.

## Effect of Ethanol-Water Composition

The effect of the ethanol-water composition on the percent recovery of damnacanthal is shown in Fig. 5. The microwave extraction was carried out for 3 min at the extraction temperature of 120°C and the

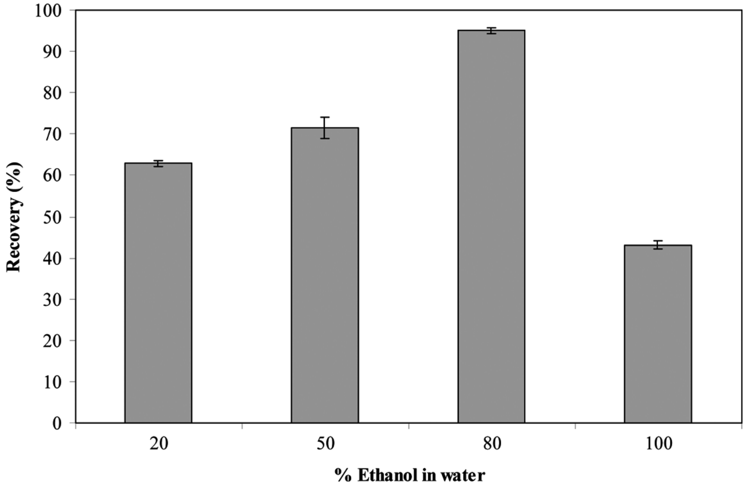

***Figure 5.*** Effect of ethanol composition on MAE efficiency of damnacanthal, material size: 0.02 mm, extraction temperature: 120°C, extraction time: 3 min, and solvent-to-sample ratio: 100.

solvent-to-sample ratio was 100. The results in Fig. 4 demonstrate that the addition of water into ethanol improved the extraction efficiency, and the highest percent recovery of damnacanthal (95%) was obtained by using 80% ethanol in water. Similar results were also reported previously in microwave-assisted extraction of antioxidative antraquinones from the roots of *Morinda citrifolia* (9). The addition of water helped increase the polarity of water as listed in Table 2 (19) and could possibly enhance the swelling of the root material, thus increasing the contact surface area between the root materials with the solvent (13). Moreover, an 80% ethanol water mixture gave the dielectric constant close to that of methanol and acetonitrile, which were previously found to be suitable solvents for the extraction of damnacanthal.

**Table 2.** Polarities of ethanol-water mixtures at various compositions

| Ethanol compositions (%) | Polarity index | Dielectric constant |
|---|---|---|
| 100 | 5.2 | 24.3 |
| 80 | 5.96 | 32.126 |
| 50 | 7.1 | 46.76 |
| 20 | 8.24 | 65.27 |

## Effect of Solvent-to-Sample Ratio

To evaluate the effect of solvent-to-sample ratio on the percent recovery of damnacanthal, a series of extractions using the sample mass of 0.1 g and different solvent volumes (5–15 ml) was carried out at 120°C for 3 minutes with 80% ethanol in water. The extracted amount of damnacanthal is shown in Fig. 6, which showed that the percent recovery of damnacanthal increased with the increase in volume of solvent, and reach the highest value when the liquid-to-solid ratio was 100. However, when a larger solvent volume was used, the percent recovery of damnacanthal no longer increased. Thus, the value of 100 was considered the optimal solvent-to-sample ratio for the MAE process.

## Comparison of Extraction Methods

The efficiency of extraction using MAE was compared with that of the other methods. Table 3 summarizes these results. For all solvent extraction methods with ethanol, 80% ethanol in water was found to give higher recovery than pure ethanol. When various extraction methods were compared using 80% ethanol in water at the extraction temperature

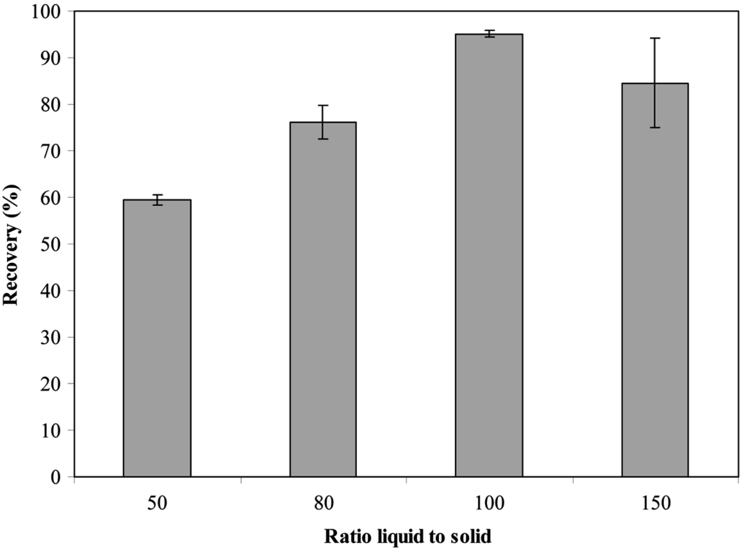

*Figure 6.* Effect of liquid-to-solid ratio on MAE efficiency of damnacanthal, material size: 0.02 mm, extraction temperature: 120°C, extraction time: 3 min, and solvent: 80% ethanol in water.

**Table 3.** Comparison of various extraction methods

| Extraction methods | Time | Temperature | Type of solvent | Recovery (%) |
|---|---|---|---|---|
| Electrical heating | 30 min | 120°C | Ethanol | 21.15 ± 0.23 |
| Electrical heating | 30 min | 120°C | Ethanol:water (80:20) | 54.64 ± 0.64 |
| UAE | 60 min | 60°C | Ethanol | 43.40 ± 0.42 |
| UAE | 60 min | 60°C | Ethanol:water (80:20) | 94.64 ± 0.25 |
| Soxhlet | 4 hr | Boiling point | Ethanol | 72.59 ± 2.26 |
| Soxhlet | 4 hr | Boiling point | Ethanol:water (80:20) | 97.22 ± 1.36 |
| MAE | 3 min | 120°C | Ethanol | 43.10 ± 1.87 |
| MAE | 3 min | 120°C | Ethanol:water (80:20) | 95.09 ± 0.67 |

120°C, MAE could most efficiently extract the compound. MAE at such conditions required only 3 min to extract 95% of damnacanthal, while 30 min was required for 55% recovery by extraction with electrical heating. With use of an 80% ethanol solution, UAE at 60°C gave a comparable percent recovery as MAE at 120°C for 3 mins; however, UAE took considerably longer (60 min versus 3 min). In addition, other advantages of MAE are the small amount of solvent and the shorter exposure time to high temperature, thus minimizing the compound degradation. From the results in this study, MAE is considered a potential alternative because of its process simplicity and lower cost compared with UAE and other conventional solvent extraction methods.

## CONCLUSIONS

In summary, MAE provides a promising alternative for extraction of the anti-cancer damnacanthal from roots of *M. citrifolia*. The appropriate condition was MAE of 0.02 mm sample at the extraction temperature of 120°C, extraction time of 3 min, and the solvent-to-sample ratio of 100. In addition to these results, the decomposition of damnacanthal was observed when the extraction time was increased after the first 5 minute irradiation time. Compared with other extraction methods such as extraction with electrical heating, soxhlet extraction, and UAE, MAE was found to give the highest extraction efficiency.

## ACKNOWLEDGEMENTS

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