



# Effects of Extraction Solvents on Red Pigment, Phenolic Compounds and Antioxidant Capacity of Red Mold Rice Extracts

Kanyaphat Apiwongsrichai<sup>1\*</sup>, Punyawatt Pintathong<sup>1,2</sup>, Phanuphong Chaiwut<sup>1,2</sup>,  
Sarita Sangthong<sup>1,2, #</sup>

<sup>1</sup> School of Cosmetic Science, Mae Fah Luang University, Chiang Rai, THAILAND

<sup>2</sup>Green Cosmetic Technology Research Group, School of Cosmetic Science, Mae Fah Luang University, Chiang Rai, THAILAND

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\*Conference presenter:  
Kanyaphat Apiwongsrichai

#Corresponding author:  
Sarita Sangthong, School of  
Cosmetic Science, Mae Fah Luang  
University, Chiang Rai, Thailand

E-mail:  
[Kanyaphat.api@mfu.ac.th](mailto:Kanyaphat.api@mfu.ac.th)  
(Kanyaphat Apiwongsrichai)

[punyawatt.pin@mfu.ac.th](mailto:punyawatt.pin@mfu.ac.th)  
(Punyawatt Pintathong)

[phanuphong@mfu.ac.th](mailto:phanuphong@mfu.ac.th)  
(Phanuphong Chaiwut)

[sarita.san@mfu.ac.th](mailto:sarita.san@mfu.ac.th)  
(Sarita Sangthong)

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## ABSTRACT

**Introduction:** Red mold rice is the rice cultivated by *Monascus* species that has long been used as natural color in traditional foods. It contains various bioactive compounds and has high potential biological activities of such antioxidant, antimicrobial and anticancer activities. It could be interesting for extraction of bioactive compounds using various solvents.

**Objective:** This research was aimed to study effects of solvents on red pigment, phenolic compounds, and antioxidant capacity of red mold rice extracts.

**Methods:** Red mold rice was prepared by cultivating *Monascus purpureus* (M. Purpureus) under solid state fermentation method. The red mold rice was extracted with different 6 different solvents, i.e., DI water, 50% ethanol, 95% ethanol, 50% acetone, acetone, and ethyl acetate. Red pigment intensity was determined by colorimetric measurement. The total phenolic, and flavonoid contents were determined by Folin-Ciocalteu, and aluminum chloride colorimetric method, respectively. The antioxidant capacity of extracts was evaluated using DPPH and FRAP.

**Results:** The result revealed that solvent types had significant effect on red pigment and phenolic compounds extractions, as well as antioxidant capacity of red mold rice extracts ( $p < 0.05$ ). The red mold rice extracted by ethyl acetate had the highest pigment intensity of  $6,526.67 \pm 100.66$  unit/g extracts. Moreover, the highest total phenolic ( $78.13 \pm 1.92$  mg GAE/g extract) and flavonoid contents ( $97.10 \pm 0.85$  mg QE/g extract) was achieved by ethyl acetate while the lowest values were gained in the presence of water. The potential antioxidant activities expressed in terms of IC<sub>50</sub> and FRAP value were reached to  $12.63 \pm 1.01$   $\mu$ g/mL, and  $180.77 \pm 7.70$  mg TEAC/g extract, respectively, in the presence of ethyl acetate.

**Conclusion:** The properties of red mold extracts were strongly influenced by the type of solvent. Among of solvent tested, ethyl acetate was considered the potential solvent providing the highest red pigment, phenolic compounds, and antioxidant capacity. There are strong correlations among red pigment, phenolic compounds, and antioxidant capacity of red mold rice extracts.

**Keywords:** *Monascus purpureus*; solid state fermentation; ethyl acetate; pigments; biological activity

## Introduction

*Monascus* spp. have long been used as natural substances through the long history in Asia. They belong to the group of Ascomycetes and particularly to the family Monascaceae. The genus *Monascus* includes four species: *M. pilosus*, *M. purpureus*, *M. ruber* and *M.*

*froridanus*, which account for the majority of strains isolated from traditional oriental foods. [1]. Among of them, *M. purpureus* is a popular strain because it possesses biological activities such as: antibacterial, antioxidant and antibiotic activities [2]. In addition, it can also produce red pigments that can be generally

produced on solid medium, especially steamed rice [3]. Red mold rice which is also known as Hongqu (in Chinese, “红曲”), red fermented rice, red yeast rice and angkak, is the fermented product of steamed rice inoculated with certain *Monascus* strains [4]. During fermentation, the red pigment is also produced by covering throughout the grains [5]. The red mold rice is composed of various chemical constituents, especially monacolins and pigments. In addition, organic acids, amino acids, sterols, decalin compound derivatives, lignans, coumarins, terpenoid, polysaccharides and flavonoid were reported as components contained in red mold rice [6]. It has been used extensively in Asia as a natural food colorant in Chinese cheese, red wine, sausage. Interestingly, it also has a potential as pharmaceutical substances and a great source of natural antioxidants [7]. In term of biological and pharmacological effects including antidiabetic effects, antifatigue effects, anti-inflammatory effects, antihypertensive effects, antihyperlipidemic effects, antioxidant effects, cholesterol-lowering effects [8] and anti-Alzheimer's effects [9]. Generally, the conventional techniques such as solid-liquid extraction have been widely used, mainly because of their efficiency, ease for manipulation [10]. Solid-liquid extraction is a method that separate one component from a mixture by dissolving it into solvent in which it is soluble while the other constituents of the mixture are not or less soluble [11]. It is generally known that the yield of extraction and biological activities of extracts depends on solvents and their concentration, the solvent/solid ratio, time of contact, temperature, and particle size of sample. Under the same conditions of extraction time, temperature and sample the solvent were found to be the important factors [12]. Solvents, such as methanol, ethanol, acetone, propanol and ethyl acetate have been commonly used for the extraction; based on the solvent's polarity and the solubility properties of compounds contained in materials [13]. Many solvents have been served for polyphenols extraction [14]. Ethanol was good solvent for polyphenol, whereas methanol has been generally found to be more efficient in extraction of lower molecular weight polyphenols. mixture solvent of water and acetone was proper for extraction of higher molecular weight flavones [15]. For flavonoid compounds, aqueous ethanol solvent performed better than aqueous methanol and aqueous acetone [16]. Another solvent, ethyl acetate was found to help to extract both polar and non-polar compounds [17,18]. This research was aimed to investigate the effects of six solvents (water, 50% ethanol, 95% ethanol, 50% acetone, acetone and ethyl acetate) on red pigments and phenolic compounds of red mold rice prepared by solid state fermentation (SSF). Additionally, antioxidant activities of the red mold rice extracts were also determined.

## Methodology

### Microorganism

*Monascus purpureus* strain TISTR3615 was obtained from TISTR Culture Collection. The microorganism was sub-cultured on Potato Dextrose Agar (PDA) and incubated at 30°C for 10 days. The mycelium was then kept in refrigerator at 4°C until use.

### Plant substrate

A 3/4 grain length of broken Jasmine rice was brought from local market. It was tightly collected in zip bags and kept in a closed plastic box at room temperature.

### Solid substrate preparation

The experiment was carried out using 250 ml size Erlenmeyer flask sealed with cotton plug. A 25 g of broken jasmine rice was mixed with DI water at solid-liquid ratio of 3:2 w/v. The rice was soaked in water for 10 min. After that, the mixture was sterilized at 121°C for 15 min using autoclave, and then allowed to cool down.

### Inoculum preparation

Spore suspension was prepared by cultivating *M. purpureus* on PDA plate for 10 days. A 2 ml of sterile Tween80® (0.1% v/v) was transferred to the culture plate. The *Monascus* colonies grown on the plate was scraped and suspended. After that, the suspension was filtrated using sterile cheese cloth. The concentration of spore was adjusted to 10<sup>6</sup> spores/ml which was counted by using heamacytometer under microscope.

### Solid state fermentation

Solid state fermentation (SSF) was performed according to Kritsadaruangchai et al. (2019) with some modifications [19]. Briefly, a 1.0 ml of spore suspension inoculum was added to the sterile solid medium, and then mixed well. The inoculated substrate was cultivated at 30°C for 10-14 days.

### Preparation of red mold rice extracts

The fermented red rice was employed for solid-liquid extraction using 6 different solvents including water, 50% (v/v) ethanol, 95% (v/v) ethanol, 50% (v/v) acetone, acetone and ethyl acetate. The ratio of solid to liquid was 1:5 w/v. An extraction was carried out on orbital shaker with 125 rpm for 3 h. After that, it was filtered and then centrifuged at 8,500 rpm at 4°C for 20 min. The solvent was removed by rotary evaporator and/or freeze dryer. The obtained crude extracts were kept at 4°C until use for determining color pigment, UV wavelength scanning, phenolic and flavonoid contents, and antioxidant activities.

#### *Determination of red pigment intensity*

Red pigment intensity was determined by the method described by Konbangkerd et al., (2014) with some modification [20]. Briefly, the sample was dissolved with appropriate solvent at different concentrations. After that, the sample solution was determined at 505 nm using visible spectrophotometer. The pigment intensity was calculated using the following equation: Pigment intensity (unit/g dry weight) = ((A505 x dilution factor x Volume of solution))/ (Weight of extract(g))

#### *Determination of wavelength scanning*

Red mold rice extract (1 mg) was solubilized into 10 mL of solution. The path length of the quartz cell used in this experiment was 1 cm. The absorbance spectrum was performed during 200 to 600 nm. [21].

#### *Determination of total phenolic content (TPC)*

Total phenolic content (TPC) was determined by Folin-Ciocalteu method as described by Lee et al (2013) with some modifications [22]. Gallic acid was used as standard. Briefly, sample solution was mixed with 0.25 mL of Folin-Ciocalteu reagent and 1.5 mL of sodium carbonate solution (7.5% w/v) respectively. After 30 min, an absorbance at 765 nm was measured using visible spectrophotometer. The TPC was expressed as Gallic acid equivalents (GAE) per g of extracts.

#### *Determination of total flavonoid content (TFC)*

Total flavonoid content (TFC) was analyzed according to the method by Lee et al (2013) with slight modification [22]. Sample solution was firstly mixed with 5% NaNO<sub>2</sub> (0.15ml), and then kept at ambient temperature for 5 min. The reaction was initiated by adding 4% NaOH (1.0 mL) and then stood for 8 min. An absorbance at 510 nm was measured using visible spectrophotometer. TFC was calculated according to a standard curve established with standard quercetin.

#### *Determination of antioxidant activity by DPPH radical scavenging activity assay*

The scavenging activity of 2,2-diphenyl-1-picrylhydrazyl (DPPH) was determined according to the method described by Sanjukta et al (2015) with some modifications [23]. Trolox was used as standard.

Sample solution was mixed with 0.1 mM DPPH reagent, and then stood in the dark at room temperature for 30 min. The absorbance was measured at 517 nm using visible spectrophotometer. The de-colorization of sample was calculated as the percentage of inhibition. The DPPH radical scavenging activity was expressed in term of milligrams Trolox equivalent antioxidant activity per gram extract (mg TEAC/g extract).

#### *Determination of antioxidant by FRAP assay*

The procedure was adapted from Benzie and Strain (1996) [24]. The reducing power of sample is based on the reduction of a ferric-tripyridyltriazine complex to produce a blue ferrous tripyridyltriazine. Trolox was used as standard. The sample was mixed with 0.3M acetate buffer (pH3.6) and FRAP reagent. The reagent was initiated by incubation at 37°C for 30 min and then the absorbance was measured at 593 nm using a visible spectrophotometer. The absorbance of a sample was also measured. The result was expressed in term of milligrams Trolox equivalent antioxidant activity per gram extract (mg TEAC/g extract).

#### *Statistical analysis*

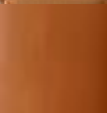
All experiments were carried out at least in triplicate, and the result were presented as mean ± SD. One-way analysis of variance (ANOVA) was used to determine significant difference ( $p < 0.05$ ), while Tukey's test for multiple comparisons, were also tested using SPSS software program (version 21).

## **Results**

#### *Pigment intensity*

The red pigment intensity of red mold rice extracted by different solvents is represented in table 1. The results demonstrated that types of extraction solvent had significant effect on red pigment intensity of the red mold rice extracts ( $p < 0.05$ ). The red mold rice extracted by ethyl acetate significantly displayed the highest red pigment value ( $6,526.67 \pm 100.66$  unit/g extract), while the lowest red pigment intensity ( $53.33 \pm 1.16$  unit/g extract) when water was employed. In addition, it was clearly observed that the red pigment intensity of red mold rice extracts was inversely proportional to polarity of solvent.

**Table 1** Red pigment intensity of red mold rice extracted by different solvents

| Solvent       | Illustration                                                                      | pigment intensity<br>(unit/g extract) |
|---------------|-----------------------------------------------------------------------------------|---------------------------------------|
| DI water      |  | 53.33 ± 1.16 <sup>a</sup>             |
| 50% Ethanol   |  | 650.67 ± 8.08 <sup>b</sup>            |
| 95% Ethanol   |  | 4,326.67 ± 83.27 <sup>c</sup>         |
| 50% Acetone   |  | 4,380 ± 69.28 <sup>c</sup>            |
| Acetone       |  | 4,733.33 ± 50.33 <sup>d</sup>         |
| Ethyl acetate |  | 6,526.67 ± 100.66 <sup>e</sup>        |

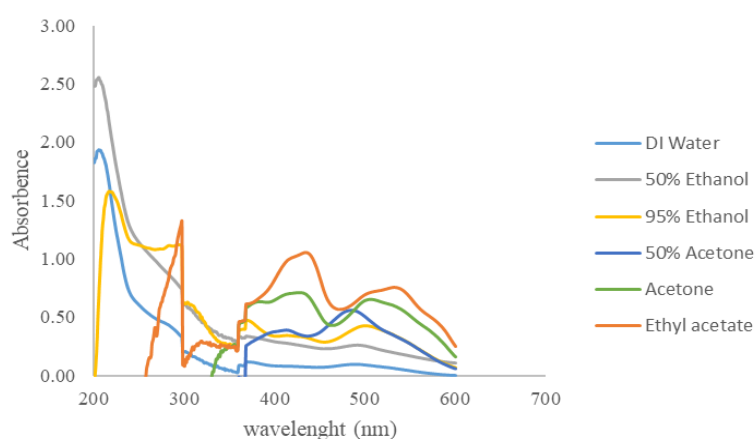
Values are given as mean ± S.D. from triplicate.

Different letters in the same column indicate a significant difference ( $p < 0.05$ ).

#### Wavelength absorption property

The wavelength scanning profiles of red mold rice extracts (0.1 mg/mL) are present in figure 1. The result revealed that ethyl acetate extract showed obviously different pattern of UV-visible absorption as compared with the other extracts. It strongly absorbed in the range of approximately 280-300 nm and 400-550 nm, while

water, 50% ethanol, and 95% ethanol extract showed a predominant absorption in the range of 200-300 nm. In contrast to acetone and 50% acetone extracts, absorption in the range of around 350-500 nm was only present. This indicated that solvents significantly affected absorption property in different UV and visible spectrum of red mold rice extracts.


**Figure 1** Wavelength scan in 200-600 nm of red mold rice extracted by different solvents

Total phenolic and flavonoid contents of the extracts from red mold rice using different extraction solvents are presented in table 2. The types of solvent had

#### Total phenolic and flavonoid contents

significant effects on phenolic and flavonoid extraction from red mold rice ( $p < 0.05$ ). The ethyl acetate extract demonstrated the highest content of phenolic and flavonoid ( $78.13 \pm 1.92$  mg GAE/g extract and  $97.10 \pm$

$0.85$  mg QE/g extract, respectively), while water was a poor solvent for extraction of phenolic ( $40.01 \pm 0.09$  mg GAE/g extract) and flavonoid ( $3.86 \pm 0.06$  mg QE/g extract).

**Table 2** Total phenolic and flavonoid contents of red mold rice extracted by different extraction solvent.

| Solvent       | TPC<br>(mg GAE/g extract) | TFC<br>(mg QE/g extract) |
|---------------|---------------------------|--------------------------|
| DI water      | $40.01 \pm 0.09^a$        | $3.86 \pm 0.06^a$        |
| 50% Ethanol   | $40.28 \pm 0.84^a$        | $26.50 \pm 0.61^b$       |
| 95% Ethanol   | $55.16 \pm 1.40^b$        | $59.55 \pm 0.77^c$       |
| 50% Acetone   | $47.79 \pm 1.66^b$        | $27.76 \pm 0.63^b$       |
| Acetone       | $67.56 \pm 0.77^c$        | $73.47 \pm 1.01^d$       |
| Ethyl acetate | $78.13 \pm 1.92^d$        | $97.10 \pm 0.85^e$       |

Values are given as mean  $\pm$  S.D. from triplicate.

Different letters in the same column indicate a significant difference ( $p < 0.05$ ).

#### Antioxidant activities

In this study, antioxidant capacity of the red mold rice extracts was evaluated based on 2 analytical methods including DPPH radical scavenging activity and FRAP. The free radical inhibition of the extracts was expressed as  $IC_{50}$  value ( $\mu\text{g/mL}$ ), while the ability to reduce ferric ion was represented as Trolox equivalent antioxidant capacity (TEAC). The values of antioxidant activity of red mold rice extracts obtained for different solvents are represented in table 3. The results showed that the red mold rice extracted by ethyl acetate significantly showed the highest  $IC_{50}$  value of  $12.63 \pm 1.01$   $\mu\text{g/mL}$  as compared with the other extracts. However, this  $IC_{50}$  value was approximately 4-fold higher than Trolox ( $3.66 \pm 0.11$   $\mu\text{g/mL}$ ). An increase of

$IC_{50}$  value was apparently observed when higher polarity of solvent was present. The highest  $IC_{50}$  value was obtained in the presence of DI water ( $57.82 \pm 2.93$   $\mu\text{g/mL}$ ), indicating the lowest antioxidant capacity. This means that antioxidant activity of the red mold rice could be decreased when using solvent used for extraction was high polarity. The FRAP values had a similar trend to the DPPH results in which ethyl acetate provided the highest FRAP value ( $180.77 \pm 7.70$  mg TEAC/g extract), while the lowest value ( $81.21 \pm 1.49$  mg TEAC/g extract) was gained in 50% ethanol extract. Therefore, it can be confirmed that types of solvent strongly had significant effect on antioxidant capacity of red mold rice extracts.

**Table 3** DPPH radical scavenging activity ( $IC_{50}$ ) and FRAP of red mold rice extracted by different solvents

| Solvent       | DPPH radical scavenging activity<br>( $IC_{50}$ , $\mu\text{g/mL}$ ) | FRAP<br>(mg TEAC/g extract) |
|---------------|----------------------------------------------------------------------|-----------------------------|
| DI water      | $57.82 \pm 2.93^g$                                                   | $81.21 \pm 1.49^b$          |
| 50% Ethanol   | $32.34 \pm 0.42^e$                                                   | $52.99 \pm 0.17^a$          |
| 95% Ethanol   | $41.08 \pm 1.74^f$                                                   | $79.68 \pm 2.31^b$          |
| 50% Acetone   | $27.44 \pm 1.27^d$                                                   | $105.22 \pm 4.89^c$         |
| Acetone       | $17.73 \pm 1.81^c$                                                   | $114.75 \pm 3.81^c$         |
| Ethyl acetate | $12.63 \pm 1.01^b$                                                   | $180.77 \pm 7.70^d$         |
| Trolox        | $3.66 \pm 0.11^a$                                                    | -                           |

Values are given as mean  $\pm$  S.D. from triplicate.

Different letters in the same column indicate a significant difference ( $p < 0.05$ ).

#### Discussion

The red mold rice extracts showed the increased red pigment intensity when extraction solvent used was low polarity. In this study, ethyl acetate displayed the highest red pigment value. The pigments of red mold rice synthesized by *M. purpureus* can be generally divided into orange (rubropunctatin and monascorubin, yellow (monascin and ankaflavin) and red (rubropunctamine and monascorubramine) [25]. Generally, red pigments are highly stable against pH, and high temperature

[26,27]. The *Monascus* pigments have a variety of physiological activities, such as antioxidant activity which is related to the pigment intensity [28]. So the pigment intensity could be an important indicator of the antioxidant activity of red mold rice extract. Ability to absorption UV-visible spectrum in the wavelength of 200-500 nm of red mold rice extracts was significant influenced by solvent used for extraction. This could be a results of different compounds represented in the different red mold rice extracts. In our studies, ethyl

acetate extract predominantly showed an absorption in the range of 350-550 nm. This could be relative with the presence of red pigment intensity in ethyl acetate extract. Koli et al. (2019) reported that combination of red pigment with chemical sunscreen increased the SPF by 36.53% and yellow pigment increased the SPF by 13.16%. The pigments may chemically interact with commercial sunscreen and undergo derivatization by making some changes in functional groups of chemical constituents present in sunscreen [29]. Phenolic components from natural sources have been suggested to play a role as natural antioxidants. Flavonoids are also potent antioxidants, free radical scavengers and they inhibit lipid peroxidation [30]. The different solvents used for extraction could lead to different compositions of phenolic compounds in extracts due to the different solubility of each phenolic compound. Consequently, the bioactivity of an extract might also be affected [31]. In this study, ethyl acetate was excellent solvent for extraction of total phenolic and flavonoids from red mold rice extract. Similar to the study of Hasim et al (2018), total phenolic and flavonoid contents in red yeast rice were highly in the presence of ethyl acetate [32]. Moreover, Zhu et al (2019) also reported that two main flavonoids found in red mold rice were daidzein and genistein [33]. The red mold rice extracts with high DPPH free radical scavenging activity exhibited higher protection against peroxidation [34]. In our study, red mold rice extracted by different solvents showed different antioxidant capacity. Among of them, the ethyl acetate extract displayed the strongest antioxidants based on the highest IC<sub>50</sub>, and FRAP values. So, it can be implied that ethyl acetate was an excellent solvent for extracting an antioxidant from red mold rice extracts. Interestingly, the high correlations of red pigment intensity, phenolic and flavonoid contents, as well as antioxidant activities can be possibly emphasized that antioxidant capacity of the red mold rice extract could be resulted from phenolic compounds and red pigment represented in the extract. As reported previously, ethyl acetate showed to be the best solvent providing the lowest IC<sub>50</sub> value assayed by DPPH Kwon (2012) [35]. Therefore, type of solvents was considered the significant factor for assessing antioxidant capacity of the red mold rice produced by *M. purpureus*. The highest antioxidant activity of *Monascus* fermented rice can perform by various antioxidant actions including reducing power, DPPH radical scavenging ability, and ferrous ions chelating ability [36].

### Conclusion

Type of solvent strongly affected red mold rice extract preparation. The highest red pigment, total phenolic and flavonoid contents, and antioxidant activities was gained when ethyl acetate was used as solvent as compared to acetone, 50% acetone, ethanol, 95% ethanol and water. An increase of solvent polarity tended to have the inverse effects. The ethyl acetate

extract highly provided red pigment intensity of  $6,526.67 \pm 100.66$  unit/g extract, while phenolic and flavonoid contents were reached at  $78.13 \pm 1.92$  mg GAE/g extract and  $97.10 \pm 0.85$  mg QE/g extract, respectively. The highest values of IC<sub>50</sub> ( $12.63 \pm 1.01$  µg/mL) and FRAP ( $180.77 \pm 7.70$  mg TEAC/g extract) indicated the potential antioxidant capacity found in the ethyl acetate extract. Moreover, strong correlations among red pigment, phenolic compounds, and antioxidant capacity were remarkably present.

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