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*Full Length Research Paper*

# Inhibitory activity of Heinz body induction *in vitro* antioxidant model and tannin concentration of Thai mimosaceous plant extracts

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**Medicinal plants have been used for traditional treatment and known to possess antioxidant activities that may help to reduce the risk of oxidative stress-related diseases. Chemically-induced oxidative hemolysis is usually associated with the formation of Heinz bodies-insoluble precipitates within red blood cells, indicating the oxidative destruction of hemoglobin. In the present study, antioxidant activity was investigated by Heinz body induction *in vitro* model for providing preliminary data selection of plant extracts compared to tannin concentration in Thai mimosaceous plant extracts. Twenty-one Thai mimosaceous plants, extracted by ethanol, were screened for tannin concentration and antioxidant activity of inhibitory Heinz body induction under *in vitro* condition. The study showed that the percentage of Heinz body inhibition activity from *Parkia speciosa* seed coat was the highest and followed by *Xylia xylocarpa* bark, *P. speciosa* pericarp, and *Entada rheedii* seed coat, respectively with inhibition concentration$_{25}$ ($IC_{25}$) of 2.68, 15.71, and 28.14 mg/ml, respectively. In addition, *X. xylocarpa* bark, *E. rheedii* seed coat and *P. speciosa* Hassk. seed coat also contained high tannin concentration. The percentage of Heinz body inhibition activity from plant extracts at dilution 1: 2 and 1: 10 (50.00 and 10.00 mg/ml) were shown correlation with tannin concentration ($p < 0.01$, $r = 0.658$ and $p < 0.05$, $r = 0.536$, respectively). This study also found that tannin could be found in all plant extracts and also inhibited the Heinz body induction at the minimum level of 0.625 mg/ml. Mimosaceous plants contained antioxidant activity demonstrated by Heinz body inhibition activity and most of the plant extracts with high Heinz body inhibition activities might be caused by high tannin concentration. This data would be valuable sources for searching potent medicine in the future.**

**Key words:** Heinz body inhibition, antioxidant, mimosaceous plant.

## INTRODUCTION

Medicinal plants have been known to have antioxidant properties which may help reduce risk of chronic diseases such as diabetes mellitus (Patra and Chua, 2011; Sharma et al., 2010), cardiovascular diseases (Karasu, 2010; Mordente et al., 2011; Ziberna et al., 2010), and cancers (Bishayee et al., 2010; Carvalho et al., 2010; Gennari et al., 2011). Thai medicinal plants have been believed to possess anti-tumor and immune-stimulating properties that may help to reduce the risk of cancers. Previous studies reported that some Thai plant extracts of mimosaceous family showed high antioxidant and α-glucosidase inhibition activities (Ramli et al., 2008; Tunsaringkarn et al., 2008). Heinz body induction is the aggregation of denatured and precipitated hemoglobin within red blood cells. Hemoglobin chains are denatured through oxidative damage by reactive oxygen species (Christopher et al., 1990) and are a useful biomarker of

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oxidative damage in the biological system (Sadighara, 2009). The presence in the blood stream of significant amounts of Heinz bodies is an evidence of some injury to the erythrocytes. If this injury is severe it may lead to marked hemolysis and anemia (Webster, 1949). In this study, twenty-one Thai plant extracts of mimosaceous family, believed to possess anti-tumor activity and maintain blood stasis, were investigated by the inhibition of Heinz body induction. However, previous report suggested that polyphenol tannic acid inhibits the hydroxide ion formation from Fenton reaction by ferrous ions (Lopes et al., 1999) and we might not seen Heinz body formation in some herbs containing high dose of tannins. Therefore, the tannin concentration of all plant extracts was investigated as standard method in parallel. An antioxidant screening model in this study might provide preliminary data to select plant extracts with the potential for oxidative stress-related disease treatment.

## MATERIALS AND METHODS

### Sample preparation

Twenty-one Thai mimosaceous plants were collected from Suansamunpri of Rachaburi and Rayong, Pathumthani garden, botanical garden of Mahidol University and Chulalongkorn University and from traditional drug stores. Dried plant samples (10 to 30 mg) were extracted by 500 ml ethanol with soxhlet apparatus and evaporated solvent with rotary evaporator. All samples were weighted and stored at 4°C until analysis.

### Sample analysis

#### *Heinz body inhibition*

Heinz body induction of plant extracts were performed in accordance with an *in vitro* model proposed by Palasuwan et al. (2005). Packed red cells (25 µl) were mixed with 500 µl of acetylphenylhydrazine solution and 500 µl of plant extracts (0.1 g/ml), and then incubated for 105 min. The Heinz body was stained by crystal violet solution at equal volume for 5 min and observed under a light microscope (1000x).

#### *Tannin analysis*

Tannin analysis was conducted following the modified method by Hagerman and Bulter (1978). All plant extracts were dissolved in 10% ethanol and 20 µL of the solution mixed in microplate with 25 µl of ferric chloride (1.6 mg/ml), added total volume to 200 µl by buffer C. Then, they incubated at 37°C for 10 min and stood for 5 min and quantified by measuring the absorbance at 510 nm by spectrophotometer.

### Statistical analysis

All parameters were expressed as mean ± S.D. Pearson's correlation were used to compare between the percentage of Heinz body inhibition and tannin concentration. The criteria for significance were $p < 0.05$.

## RESULTS

The scientific names, Thai names, part used, and percentage yield of plant extracts were shown in Table 1. *Xylia xylocarpa* (Roxb.) Taub.bark has the highest yield, followed by *Adenanthera pavonina* L. leaves, *X. xylocarpa* (Roxb.) Taub. leaves, *Samanea saman* (Jacq.) Merr. Leaves and *Acacia catechu* (L.f.) Wild leaves at 22.69, 20.72, 19.44, 17.88, and 16.38 %, respectively. The most yield of plant extracts were those of leaves. The percentage of Heinz body formation and total tannin concentration of plant extracts were shown in Table 2. The extracts from *Parkia speciosa* Hassk. seed coat, *X. xylocarpa* (Roxb.) Taub. bark, *P. speciosa* Hassk. pericarp, *Entada rheedii* Spreng. seed coat, *Albizia lebbeckoides* (DC.) Benth. bark, *Pithecellobium dulce* Benth. bark and *Cathormion umbellatum* (Vahl.) leaves have shown high activity of Heinz body inhibition (39.98, 42.75. 44.89, 55.12, 58.90, 61.61, 79.71 and 86.14%, respectively at dilution 1:2 or 50 mg/ml) (Figure 1). *P. speciosa* Hassk. seed coat, *X. xylocarpa* (Roxb.) Taub. bark, *P. speciosa* Hassk. pericarp, *C. umbellatum* (Vahl.) bark, *E. rheedii* Spreng. seed coat may have a high sequence of strong inhibition respectively. *X. xylocarpa* bark, *E. rheedii* seed coat, *P. speciosa* Hassk. seed coat, and *X. xylocarpa* stem contained high tannin concentration, respectively (Table 2).

The $IC_{25}$ of *P. speciosa* Hassk. seed coat, *X. xylocarpa* (Roxb.) Taub. bark, *P.speciosa* Hassk. pericarp, *C. umbellatum* (Vahl.) bark, *A. lebbeckoides* (DC.) Benth. bark, *P. dulce* Benth. bark and *C. umbellatum* (Vahl.) leaves were 2.68, 15.71, 28.14, 30.46, 36.05, 59.36, and 82.15 mg/ml, respectively (Table 3); while $IC_{50}$ of *P. speciosa* Hassk. seed coat, *X. xylocarpa* (Roxb.) Taub. bark, *P. speciosa* Hassk. pericarp and *C. umbellatum* (Vahl.) bark were 3.90, 40.89, 46.29, and 50.92 mg/ml, respectively. For standard tannin, it was able to completely inhibit the Heinz body formation from dilution 1:2 to 1:40 which could be found in all plant extracts while $IC_{25}$ and $IC_{50}$ of standard tannin were at 0.74 and 0.91.mg/ml (Figure 2 and Table 3).

Pearson's correlation showed high correlation between the percentage of Heinz body inhibition of plant extracts and tannin concentration ($p < 0.01$, $r = 0.658$ at extract dilution 1:2 and $p < 0.05$, $r = 0.536$ at extract dilution 1:10).

## DISCUSSION

Mimosaceae is one of the thirty-four families like some fruits and vegetables which can be found in culinary plants such as *Acacia farnesana* (Linn.) Welld, *P. dulce* Benth. and *P. speciosa* Hassk. In addition, some plants are used for traditional medicine, such as *Albizia procera* (Roxb.) Benth. and *X. xylocarpa* (Roxb.) Taub. Some studies have shown high antioxidant activities of *X.*

**Table 1.** Scientific names, Thai names, part used and plant extraction yield percentage.

| Scientific name of plants | Thai name | Part used | % Yield of plant extractions [a] (w/w) |
|---|---|---|---|
| *Acacia catechu* (L.f.) Willd. | Sisied | Branch | 2.70 |
| *Acacia catechu* (L.f.) Willd. | Sisied | Leaves | 16.38 |
| *Albizia lebbeckoides* (DC.) Benth. | Kang | Bark | 11.04 |
| *Albizia lebbeckoides* (DC.) Benth. | Kang | Branch | 3.93 |
| *Acacia farnesana* (Linn.) Welld. | Krathinhom | Twig | 15.52 |
| *Adenanthera pavonina* L. | Maglumtachang | Leaves | 20.72 |
| *Albizia lebbeck* (L.) Benth. | Chamjureesithong | Branch | 3.40 |
| *Albizia procera* (Roxb.) Benth. | Tington | Bark | 8.18 |
| *Archidendron jiringa* I.C. Nielsen | Lookneang | Seed coat | 9.01 |
| *Cathormion umbellatum* (Vahl.) | Ragumpa | Bark | 11.41 |
| *Cathormion umbellatum* (Vahl.) | Ragumpa | Leaves | 11.25 |
| *Entada rheedii* Spreng. | Sabamon | Seed coat | 4.72 |
| *Entada rheedii* Spreng. | Sabamon | Pericarp | 1.60 |
| *Pithecellobium dulce* Benth. | Makamtet | Bark | 3.94 |
| *Parkia speciosa* Hassk. | Sataw | Pericarp | Do not weight |
| *Parkia speciosa* Hassk. | Sataw | Seed coat | 19.17 |
| *Samanea saman* (Jacq.) Merr. | Kampu | Branch | 4.46 |
| *Samanea saman* (Jacq.) Merr. | Kampu | Leaves | 17.88 |
| *Xylia xylocarpa* (Roxb.) Taub. | Maidang | Bark | 22.69 |
| *Xylia xylocarpa* (Roxb.) Taub. | Maidang | Leaves | 19.44 |
| *Xylia xylocarpa* (Roxb.) Taub. | Maidang | Stem | 4.10 |

[a] Percentage extract yield (W/W) was calculated as (dry extract weight/dry weight material) × 100.

**Table 2.** Heinz body formation and tannin concentration in plant extracts.

| Plant extract | % of Heinz body formation in serial dilution [b] | | | | | Total tannin concentration (mg/g plant extract) |
|---|---|---|---|---|---|---|
| | 1:2 (50 mg/dl) | 1:10 (10 mg/dl) | 1:20 (5 mg/dl) | 1:40 (2.5 mg/dl) | 1:80 (1.25 mg/dl) | |
| *Acacia catechu* (L.f.) Willd. branch | 100.00 | 100.00 | 100.00 | 100.00 | 100.00 | 33.00 |
| *Acacia catechu* (L.f.) Willd. leaves | 100.00 | 100.00 | 100.00 | 100.00 | 100.00 | 167.00 |
| *Albizia lebbeckoides* (DC.) Benth. bark | 61.61 | 100.00 | 100.00 | 100.00 | 100.00 | 150.00 |
| *Albizia lebbeckoides* (DC.) Benth. branch | 100.00 | 100.00 | 100.00 | 100.00 | 100.00 | 17.00 |
| *Acacia farnesana* (Linn.) Welld. twig | 100.00 | 100.00 | 100.00 | 100.00 | 100.00 | 58.00 |
| *Adenanthera pavonina* L. leaves | 100.00 | 100.00 | 100.00 | 100.00 | 100.00 | 1.70 |
| *Albizia lebbeck* (L.) Benth. branch | 100.00 | 100.00 | 100.00 | 100.00 | 100.00 | 6.70 |
| *Albizia procera* (Roxb.) Benth.bark | 100.00 | 100.00 | 100.00 | 100.00 | 100.00 | 50.00 |

**Table 2.** Contd.

| | | | | | | |
|---|---|---|---|---|---|---|
| *Archidendron jiringa* I.C. Nielsen seed coat | 100.00 | 100.00 | 100.00 | 100.00 | 100.00 | 83.00 |
| *Cathormion umbellatum* (Vahl.) bark | 51.12 | 100.00 | 100.00 | 100.00 | 100.00 | 167.00 |
| *Cathormion umbellatum* (Vahl.) leaves | 86.14 | 100.00 | 100.00 | 100.00 | 100.00 | 250.00 |
| *Entada rheedii* Spreng. seed coat | 58.9 | 100.00 | 100.00 | 100.00 | 100.00 | 400.00 |
| *Entada rheedii* Spreng. pericarp | 100.00 | 100.00 | 100.00 | 100.00 | 100.00 | 250.00 |
| *Pithecellobium dulce* Benth. bark | 79.71 | 100.00 | 100.00 | 100.00 | 100.00 | 133.00 |
| *Parkia speciosa* Hassk. pericarp | 44.89 | 100.00 | 100.00 | 100.00 | 100.00 | 250.00 |
| *Parkia speciosa* Hassk. seed coat | 39.98 | 75.00 | 100.00 | 100.00 | 100.00 | 350.00 |
| *Samanea saman* (Jacq.) Merr. branch | 100.00 | 100.00 | 100.00 | 100.00 | 100.00 | 42.00 |
| *Samanea saman* (Jacq.) Merr. leaves | 100.00 | 100.00 | 100.00 | 100.00 | 100.00 | 17.00 |
| *Xylia xylocarpa* (Roxb.) Taub. bark | 42.75 | 64.50 | 100.00 | 100.00 | 100.00 | 400.00 |
| *Xylia xylocarpa* (Roxb.) Taub. leaves | 100.00 | 100.00 | 100.00 | 100.00 | 100.00 | 167.00 |
| *Xylia xylocarpa* (Roxb.) Taub. stem | 100.00 | 100.00 | 100.00 | 100.00 | 100.00 | 350.00 |
| Standard Tannin | 0.00 | 0.00 | 0.00 | 0.00 | 12.45 | - |

[b] % Heinz body formation was observed in at least 1000 red blood cells under a microscope (1000x).

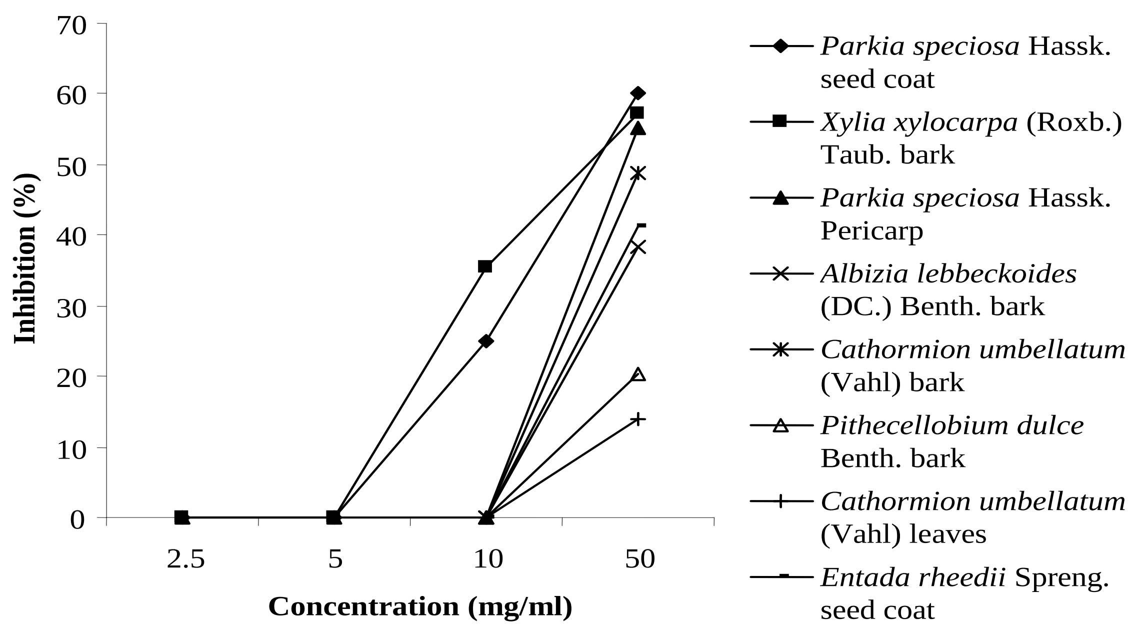


**Figure 1.** Heinz body inhibition of plant extracts.

**Table 3.** $IC_{25}$ and $IC_{50}$ of plant extracts and standard tannin.

| Plant extract | $IC_{25}$ (mg/ml) | $IC_{50}$ (mg/mL) |
|---|---|---|
| *Parkia speciosa* Hassk. seed coat | 2.68 | 3.90 |
| *Xylia xylocarpa* (Roxb.) Taub. bark | 15.71 | 40.89 |
| *Parkia speciosa* Hassk. pericarp | 28.14 | 46.29 |
| *Cathormion umbellatum* (Vahl.) bark | 30.46 | 50.92 |
| *Entada rheedii* Spreng. seed coat | 33.20 | - |
| *Albizia lebbeckoides* (DC.) Benth.bark | 36.05 | - |
| *Pithecellobium dulce* Benth. bark | 59.36 | - |
| *Cathormion umbellatum* (Vahl.) leaves | 82.15 | - |
| Standard Tannin | 0.74 | 0.91 |

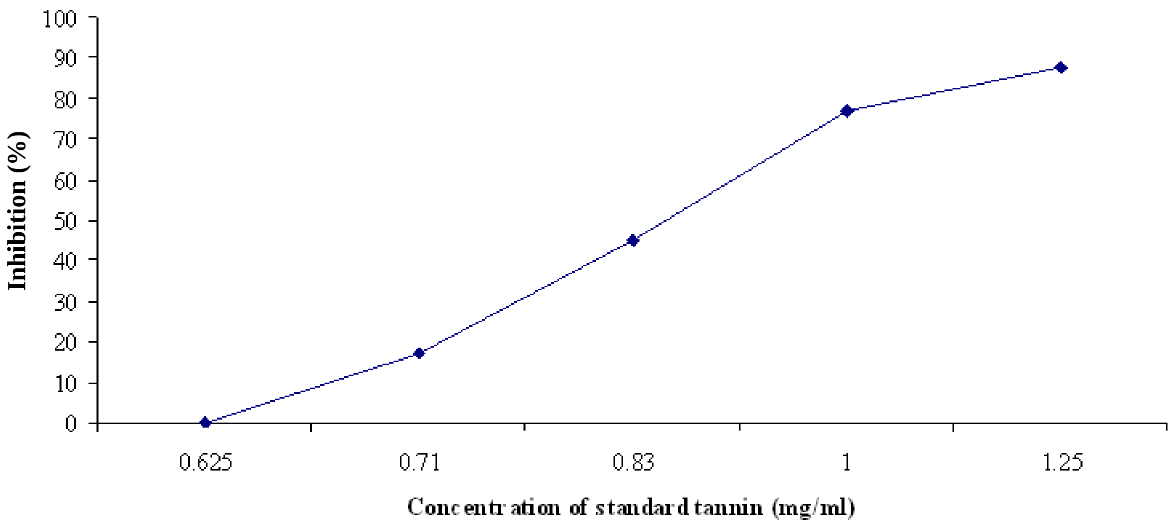


**Figure 2.** Heinz body inhibition of standard tannin.

*xylocarpa* (Roxb.) Taub., *E. rheedii* Spreng., *Archidendron jiringa* I.C. Nielsen., and *P. speciosa* Hassk. by DPPH and ABTS superoxide anion radical scavenging activities *in vitro* model (Jongjareonrak et al., 2008; Ramli et al., 2008). The present study demonstrated that Heinz body inhibition activity for effect-tive plant extract screening in relation to the susceptibility of red blood cell to the oxidative stress. The result showed that *P. speciosa* Hassk. seed coat, *X. xylocarpa* (Roxb.) Taub. bark, *P. speciosa* Hassk. pericarp, *C. umbellatum* (Vahl.) bark and *E. rheedii* Spreng. seed coat at dilution 1:2 or 50.00 mg/ml had high Heinz body inhibition, respectively. In addition, the $IC_{25}$ and $IC_{50}$ confirmed that *P. speciosa* Hassk. seed coat, *X. xylocarpa* (Roxb.) Taub. bark, *P. speciosa* Hassk. pericarp and *C.umbellatum* (Vahl.) bark were a sequence of inhibition activity. *P. speciosa* Hassk. or '*sataw*'-Thai common names, is widely found and used as traditional food in Southeast Asia including Indonesia, Brunei, the Northern part of Malaysia, and the Southern part of Thailand. Lectin are the constituent of *P. speciosa* seed, determined by denaturizing gel electrophoresis (Suvachittanont and Peutpaiboon, 1992). The lectin from *P. speciosa* seeds has mitogenic activity by stimulating incorporation of [3H] thymidine into DNA of rat thymocytes (Suvachittanont and Jaranchavanapet, 2000). The earlier report also showed that lectin from *P. speciosa* seed has hemagglutinating activity (Chankhamjon et al., 2010).

In this study, tannin had very strong Heinz body inhibition with $IC_{25}$ and $IC_{50}$ at 0.74 and 0.94 mg/ml and was found in all samples of plant extracts with higher levels than minimum concentration of inhibition (0.625 mg/ml). Our study also found high correlation between the percentage of Heinz body inhibition and tannin concentration. Therefore, the Heinz body inhibition might be caused by active ingredient interaction and also tannin interference. There were many natural plants containing high dose of tannin (Lopes et al., 1999; Nakagawa and Yokozawa, 2002). The previous results suggested that the antioxidant activity of tannin was mainly due to iron chelation rather than hydroxide radical scavenging (Lopes et al., 1999). Therefore, tannin could be used for cancer chemotherapy (Tikoo et al., 2011).

In conclusion, this study proposed that *P. speciosa* Hassk. seed coat and *X. xylocarpa* (Roxb.) Taub. bark have high antioxidant activities which may be effective to protect human against free radicals, one of the causes of chronic diseases (Jomova et al., 2010; Kashihara et al., 2010; Kang et al., 2011; Munakata et al., 2011; Tang et al., 2011). Most of the extracts of Thai mimosaceous plants which contained high Heinz body inhibition activity might be caused from high tannin concentration. This study provides the data of Thai mimosaceous plants which would be valuable sources for searching potent medicine in the future.

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