



Anti-inflammatory Activity of Isolated Flavonoid from *Sida cordifolia* Leaves Extract

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ABSTRACT

The anti-inflammatory activities of *Sida cordifolia* leave extract were scientifically stated. However, no report has yet been published about the active component responsible for anti-inflammatory activity of *Sida cordifolia* leaves extract. It was intended to isolate the flavonoids from the *Sida cordifolia* leaves extract and investigated its anti-inflammatory efficacy. Petroleum ether and ethanol extract were extracted out from the powdered of leaves. The phytochemical study was done for both extracts. The *in vitro* antioxidant activity was performed on ethanol extract on different models. The column chromatography was used for the isolation of flavonoid from ethanol extract, and further anti-inflammatory potency of the isolated compound was investigated. The phytochemical study indicates flavonoids and polyphenol were present in ethanol extract. The higher antioxidant activity was observed in ethanol extract from findings of antioxidant study. The isolated flavonoids exhibited R_f value of 0.46 on solvent ratio of chloroform: methanol (1:1), which was similar to standard quercetin. The significant anti-inflammatory activity was found for isolated flavonoid against carrageenan-induced edema and cotton pellet-induced granuloma in experimental animals. The findings confirmed that the flavonoid present in the *Sida cordifolia* demonstrated anti-inflammatory activity.

Keywords: *Sida cordifolia*, Flavonoids, Anti-inflammatory activity, Carrageenan-induced edema, Cotton pellet-induced granuloma

INTRODUCTION

Throughout the most recent decade, incredible advancement has been made in comprehension the physiopathology of inflammation and association of free radicals in its pathogenesis. The receptive oxygen species (ROS) created from the activity of free radicals on molecular oxygen increment strangely during inflammation, causing an imbalance between the oxidizing molecules and the antioxidant system of the body. Oxidative stress origins inflammatory cascades that harm the cellular components [1,2]. The inflammation that is unconstrained leads to chronic inflammatory disorders. The inflammation occurs due to granuloma formation and leukocyte infiltration. The flavonoids existing in the plant imparts prominent anti-inflammatory properties. The flavonoids easily hinder the creation of free radical and control the inflammation [3].

Presently, synthetic drugs are ruling the market however component of danger that these medications involve, can't be discounted. Their delayed use may cause severe adverse effects for endless administration the most well-known being gastrointestinal bleeding and peptic ulcers. Consequently, there is a need to build up new anti-inflammatory drugs with minimum side effects. Search for safe and effective anti-inflammatory agents have been given priority in scientific research in the herbal system of medicine [4].

Sida cordifolia is used to treat bronchial asthma, cold and flu, chills, lack of perspiration, headache, nasal congestion, aching joints and bones, cough and wheezing, and edema. *Sida cordifolia* has scientifically reported the anti-inflammatory, anti-cancer, antibacterial and antidepressant activities [5-7]. Further 4 new alkaloids have been isolated from methanol extract of aerial parts of *Sida cordifolia* viz., 1,2,3,9-tetrahydro-pyrrolo [2,1-b] quinazolin-3-ylamine, 5'-hydroxymethyl-1'-(1,2,3,9-tetrahydro-pyrrolo [2,1-b] quinazolin-1-yl)-heptan-1-one, 2-(1'-amino-butyl) indol-3-

one, and 2'-(3H-indol-3-ylmethyl)-butane-1'-ol [8,9]. The 3 new flavonol C-glycosides: 3'-(3'',7''-dimethyl-2'',6''-octadiene)-8-C-β-D-glucosyl-kaempferol-3-O-β-D-glucoside, 3'-(3'',7''-dimethyl-2'',6''-octadiene)-8-C-β-D-glucosyl-kaempferol 3-O-β-D-glucosyl [1-4]-α-D-glucoside, and 6-(3''-methyl-2''-butene)-3'-methoxyl-8-C-β-D-glucosyl-kaempferol 3-O-β-D-glucosyl [1-4]-β-D-glucoside has been reported [10]. Two new bioactive flavones of 5,7-dihydroxy-3-isoprenyl flavone and 5-hydroxy-3-isoprenyl flavone were isolated from the chloroform extract of *Sida cordifolia* [11].

The anti-inflammatory activities of *Sida cordifolia* leave extract were scientifically reported. However, no report has yet been published about the active component responsible for the anti-inflammatory activity of *Sida cordifolia* leaves extract. The objective of the present study was to evaluate the anti-inflammatory activity of flavonoids compound present in *Sida cordifolia* leaves extract.

MATERIALS AND METHODS

Preparation of Extract

The petroleum ether and ethanol extract of leaves of *Sida cordifolia* were prepared by soxhlet apparatus.

Phytochemical Tests

Phytochemical screening was done on petroleum ether and ethanol extract to detect the nature of phytoconstituents present in the extract [12,13].

In vitro Antioxidant Activity of Extract

Hydrogen-donating activity: The methanol solution of DPPH (100 mM, 2.95 ml), 0.05 ml of extracts broke up in methanol was included at a various concentration (50-250 μg/ml). The response blend was shaken and after 30 min at room temperature, the absorbance esteems were estimated at 517 nm and changed over into a level of cellular antioxidant activity (%AA). Ascorbic acid was utilized as a standard. The level of staining demonstrates the rummaging adequacy of the extract, which was determined by the following equation [3]:

$$\%AA = 100 - \left\{ \left[\left(Abs_{sample} - Abs_{blank} \right) \times 100 \right] / Abs_{DPPH} \right\}$$

The IC₅₀ parameter of ethanol extracts was determined using Microsoft Excel 2007.

Total polyphenol content (TPC): Total polyphenol content was resolved utilizing the colorimetric technique. The solution 1.0 ml was oxidized by adding 2.5 ml of Folin-Ciocalteu reagent, and 2.0 ml of sodium carbonate solution (75 g/l). The solution of absorbance was measured at 760 nm. The amount was calculated using the Gallic acid calibration curve [3]. The results were expressed as Gallic acid equivalent (GAE) mg per 100 ml of the sample (extract).

Total flavonol content (TPC): The 9.8 ml of the readied extract was blended with a 10% aluminum chloride solution (200 μl). The absorption of the solution was estimated at a 425 nm wavelength after 30 min. The sum was determined to utilize the quercetin calibration curve [3]. The outcomes were communicated as the quercetin equal (QE) mg per 100 ml of the sample.

Reducing power assay: The ethanol extract and ascorbic acid were broken up independently in 1.0 mL of distilled water with phosphate buffer (2.5 mL, 0.2 M, pH 6.6), and added 1% potassium ferricyanide (2.5 mL). The blend was brooded at 50°C for 20 min. Aliquots of trichloroacetic corrosive (2.5 mL, 10% w/v) were added to the blend and centrifuged at 3000 rpm for 10 min. The 2.5 ml of solution was separated and mixed with the same quantity of distilled water. After that newly prepared 0.5 ml of 0.1% FeCl₃ solution was added to the mixture. The absorbance of the solution was estimated at 700 nm³.

Isolation of Flavonoid from Ethanol Extracts

The *Sida cordifolia* extract was subjected to column chromatography using silica gel (60-120 mesh size), and eluted with the following solvent ratios of Ethyl acetate (EA): Ethanol (Eth), 100:0, 90:10, 80:20, 70:30, 60:40, 50:50, 40:60, 30:70, 20:80, 10:90, 0:100. The fractions (25 ml) were collected from the column. The elute collected were monitored by thin-layer chromatography [eluent: chloroform: methanol (1:1)] for homogeneity and the similar fraction were pooled together. Column fractions from 45 to 52 with ethyl acetate: ethanol (80:20) in the TLC mobile phase solvent

ratio of chloroform: methanol (1:1) showed R_f value of 0.46 equal to that of standard quercetin. The fractions were then combined and crystallized and the final yield approximately 100 mg and was considered as isolated flavonoids [14]. This process was repeated several times by using the bulk quantity of samples until the desired amount of quercetin has been obtained.

Anti-Inflammatory Activity

Anti-inflammatory activity of isolated flavonoids on carrageenan-induced edema: The albino Wistar rats of either sex weighing between (150-200 gm) were partitioned into different gatherings and 6 animals in each group:

- Group I (control group) received distilled water
- Group II received standard drug indomethacin at 10 mg/kg body weight
- Group III received isolated flavonoid at 50 mg/kg body weight
- Group IV received isolated flavonoid at 100 mg/kg body weight

Acute inflammation was created by injecting 0.1 ml of 1% carrageenan suspension in normal saline into the sub-plantar area of right hind paw following an hour of medication organization. The control gathering was directed to just distilled water. The confined compound and standard medications controlled intraperitoneally 1 h before carrageenan suspension administration.

An imprint was made on the leg at the malleolus to encourage uniform plunging at resulting readings. The volume of paw edema volume was estimated with the assistance of plethysmograph by mercury removal strategy preceding and 5 hours after the medication administration [15,16]. The restraint of edema in different treated gatherings was then determined by utilizing statistical examination

Anti-inflammatory activity of isolated flavonoids on cotton pellet-induced granuloma model: The albino Wistar rats of either sex weighing between (150-200 gm) were partitioned into different gatherings and 6 animals in each group:

- Group I (control group) received distilled water
- Group II received standard drug indomethacin at 10 mg/kg body weight
- Group III received isolated flavonoid at 50 mg/kg body weight
- Group IV received isolated flavonoid at 100 mg/kg body weight

Sterile cotton pellets each gauging 30 ± 5 mg were arranged and sanitized in a sight-seeing oven at 123°C for 3 h. Every rat was put under light ether anesthesia and subcutaneously embedded with four cotton pellets, one each into both the axillae and the crotch area under aseptic conditions. The medications were managed orally for 7 days beginning from the day of implantation of the pellets. Every one of the rats had free access to drinking water and nourishment. On the 8th day, every one of the rats was relinquished and the embedded cotton pellets were recuperated, cleaned of encompassing tissues, and smeared with channel paper [3]. These cleaned pellets were gauged and dried in a tourist oven medium-term at 70°C and the dry loads were noted.

Statistical Analysis

The outcomes are communicated as mean \pm SEM of 6 autonomous investigations. Measurable significance between the gatherings was assessed by one-way analysis of variance (ANOVA) trailed by Dunnet's test. A $p < 0.05$ worth was considered as statistically significant.

RESULTS AND DISCUSSION

Phytochemical Screening

The fat and oil gave the positive test in petroleum ether extract of leaves of *Sida cordifolia*, while glycosides, tannins, alkaloids, flavonoids, carbohydrates, proteins, and polyphenol were present in ethanol extract. The ethanol extract was selected for further study due to the existence of flavonoids and polyphenol in the extract.

Hydrogen-Donating Activity

Table 1 demonstrated that the DPPH radical was neutralized by ethanol extract and ascorbic acid with IC₅₀ value 92.84 µg/ml and 48.13 µg/ml, respectively. The scavenging properties of ethanol extract and ascorbic acid were found to dose-dependent.

Table 1 Free radical scavenging capacity of *Sida cordifolia* ethanol extracts and ascorbic acid

Concentration (µg/ml)	DPPH Scavenging (%)	
	Ethanol Extract	Ascorbic Acid
50	32.6 ± 1.19	49.3 ± 0.73
100	51.2 ± 1.62	86.1 ± 0.28
150	73.5 ± 1.43	138.7 ± 0.39
200	102.4 ± 0.84	172.8 ± 0.51
250	123.7 ± 1.08	201.5 ± 0.66
IC ₅₀	92.84	48.13

Data are expressed as mean ± SEM of six determinations

TPC and TFC

The TPC and TFC of ethanol extract of *Sida cordifolia* were 74.61 mg/gm and 78.24 QE mg/gm, respectively (Table 2). The ethanol extract of *Sida cordifolia* has a higher quantity of TPC and TFC.

The flavonoid found in the plant is an extraordinary wellspring of medications and utilized for the treatment of different sorts of diseases related to free radical. The flavonoids and polyphenol neutralized the free radical generated by the oxidative stress and control the diseases [17,18]. The results of TPC and TFC of ethanol extract of *Sida cordifolia* sustains the investigation of DPPH neutralizing capacity of extracts.

Table 2 Data of TPC and TFC of *Sida cordifolia* extract

Extract	Total Polyphenol Content (GAE mg/gm)	Total Flavonol Content (QE mg/gm)
Ethanol extract	74.61 ± 0.69	78.24 ± 1.39

Data are expressed as mean ± SEM of 6 determinations

Reducing Power Assay

Table 3 exhibited the strong reducing power properties of ethanol extract and its value was 64.56%.

Table 3 Antioxidant activity determination of *Sida cordifolia*

Particulars	Absorbance at 700 nm	Antioxidant Activity (%)
Ascorbic acid	0.793±0.28	100
Ethanol extract	0.512±0.92	64.56

Data are expressed as mean ± SEM of 6 determinations

The extent of hydrogen contributing capability of substance is responsible for their reducing property. Hence this validates that ethanol extract of *Sida cordifolia* consisting the extreme extent of the polyphenol and flavonoid. The outcomes expressed that extract goes about as electron donors and could respond with free radicals to change over them into increasingly stable items and afterward end the free radical chain responses. During the study, it was established that antioxidant activity was created because of the existence of flavonoids in the extract. Hence the ethanol extract of *Sida cordifolia* was designated for the separation of flavonoid by column chromatography.

Flavonoid Isolated from Extracts

The ethanol extract of *Sida cordifolia* was imperiled to column chromatography and fractions were eluted with the gradient polarity of ethyl acetate and ethanol. Column fractions from 48-54 with ethyl acetate: ethanol (80:20) in the TLC mobile phase solvent ratio of chloroform: methanol (1:1) showed R_f value of 0.46 equal to that of standard quercetin. Hence the isolated flavonoid might be considered as quercetin compound.

Anti-Inflammatory Activity

The *in vitro* examination of the isolated flavonoids from *Sida cordifolia* leaves extracts expressed the presence of quercetin compound. Therefore anti-inflammatory activity was performed with isolated flavonoid.

Carrageenan-induced edema: The anti-inflammatory efficacy of the isolated flavonoid of *Sida cordifolia* against carrageenan-induced paw edema is obtainable in Table 4. The local edema of animals of control group enhanced gradually after the sub-plantar injection of carrageenan. The significant lessening in edema in the rats was observed after administration of isolated flavonoid. Consequently, indomethacin created a significant reduction in edema in rats.

Table 4 Anti-inflammatory activity of isolated flavonoids on carrageenan-induced paw edema

Treated Group	Paw volume after induction				
	1 hr	2 hr	3 hr	4 hr	5 hr
Control	0.23 ± 2.19	0.58 ± 1.34	0.79 ± 1.65	1.14 ± 1.84	1.02 ± 2.48
Indomethacin (10 mg/kg)	0.22 ± 0.63	0.31 ± 2.03*	0.36 ± 1.28*	0.29 ± 1.41*	0.20 ± 2.35*
Isolated Flavonoids (50 mg/kg)	0.25 ± 1.41	0.46 ± 2.56	0.57 ± 2.37*	0.51 ± 1.17*	0.39 ± 1.78*
Isolated Flavonoids (50 mg/kg)	0.24 ± 1.92	0.41 ± 1.73	0.48 ± 1.47*	0.42 ± 1.58*	0.28 ± 1.14*

Data are stated as mean ± SEM, *p<0.05 significant difference compared to the control group

Carrageenan-induced edema is a suitable model for estimating the anti-inflammatory properties of the extract obtained from plants and is supposed to be biphasic. The first stage which happens inside an hour is accepted to include the arrival of serotonin and histamine while the second stage which happens following 1 hr has been credited to prostaglandin and the progression between the 2 stages is given by kinin [19]. That the flavonoid isolated from extract created anti-inflammatory impact 2 hrs post-carrageenan infusion proposes that its anti-inflammatory properties may include the restraint of prostaglandin union and cyclooxygenase items since the carrageenan inflammatory model fundamentally mirrors the activity of prostaglandins. The isolated flavonoid anticipated the development of exudate and leucocytes activation incited by intraperitoneal injection of carrageenan [20,21]. The inhibitory impact of the isolated flavonoid on the intraperitoneal development of exudate and leucocytes assembly is likely because of the hindrance of prostaglandins. This prospect is fortified by the way that the isolated flavonoid amazingly hindered paw oedematous process which is accepted to be intervened by prostaglandins.

The calming impacts documented for isolated flavonoid of *Sida cordifolia* in this examination brought about by the all-out polyphenol and flavonoids constituents present in the plants. Be that as it may, the system of these activities is questionable, and the flavonoids and polyphenol impart chief role for the anti-inflammatory activity.

Cotton pellet-induced granuloma model: The anti-inflammatory effect of flavonoids isolated from *Sida cordifolia* extract was studied. The significant decrease in weight of wet and dry cotton pellets was observed after administration of isolated flavonoids to rats (Table 5). Similar results were seen in standard drug-treated rats.

Table 5 Anti-inflammatory properties of isolated flavonoids on cotton pellet-induced granuloma rats

Group	Wet Weight (mg)	Inhibitions (%)	Dry Weight (mg)	Inhibitions (%)
Control	356.14 ± 2.68	-	93.21 ± 1.84	-
Indomethacin (10 mg/kg)	152.47 ± 2.45*	57.18	23.71 ± 2.39*	74.56
Isolated flavonoids (50 mg/kg)	223.73 ± 2.31*	37.17	35.15 ± 2.57*	62.28
Isolated flavonoids (50 mg/kg)	192.35 ± 1.72*	45.99	29.42 ± 2.11*	68.43

Data are stated as mean ± SEM, *p<0.05 significant difference compared to the control group

The cotton-pellet granuloma model is broadly used to explore the transudative and proliferative parts of the chronic inflammation. In this study wet weight of the pellets correlates with transude, and the dry weight of the pellet compares with the number of granulomatous tissues [22]. Chronic inflammation happens by methods for the advancement of multiple cells. The inflammation included multiplication of macrophages, neutrophils, and fibroblast, which are essential wellsprings of granuloma development. The affected cells can be either spread or in granuloma structure. The drugs of non-steroidal anti-inflammatory decline the extent of granuloma which consequences from cell response by restraining granulocyte invasion, avoiding the age of collagen filaments and smothering mucopolysaccharides [23]. The isolated flavonoid of *Sida cordifolia* demonstrated significant anti-inflammatory activity in cotton pellet instigated granuloma and along these lines observed to be effective in chronic inflammatory conditions, which mirrored its adequacy in hindering the expansion in the number of fibroblasts and union of collagen and mucopolysaccharides during granuloma tissue formation.

Flavonoids have been perceived to have anti-inflammatory properties, both *in vitro* and *in vivo* [24,25]. The above

study established that isolated flavonoid obtained from *Sida cordifolia* leaves extract are accountable for its anti-inflammatory activity and the impacts examined are inferable because of the nearness of flavonoids in the plant.

CONCLUSION

The current study was made to isolate the flavonoid compound from *Sida cordifolia* leaves extract and assess their anti-inflammatory activity. The ethanol extract expressed extreme antioxidant property. The isolated flavonoid of *Sida cordifolia* leaves extracts exhibited significant anti-inflammatory activity. The findings suggest the anti-inflammatory activity of *Sida cordifolia* is due to the presence of flavonoids in the extract. Further investigations are conveyed for the conceivable mechanism and the identification of the isolated flavonoid accountable for anti-inflammatory activity.

DECLARATIONS

Conflict of Interest

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

REFERENCES

- [1] Amri, Oukacha, et al. "Anti-inflammatory activity of methanolic extract from *Pistacia atlantica* Desf. leaves." *Pharmacognosy Journal*, Vol. 10, No. 1, 2018, pp. 71-76.
- [2] Seril, Darren N., et al. "Oxidative stress and ulcerative colitis-associated carcinogenesis: Studies in humans and animal models." *Carcinogenesis*, Vol. 24, No. 3, 2003, pp. 353-62.
- [3] Sarkar, A., V. D. Tripathi, and R. K. Sahu. "Anti-inflammatory and anti-arthritis activity of flavonoids fractions isolated from Centipede minima leaves extracts in rats." *Clinical and Experimental Pharmacology*, Vol. 7, No. 231, 2017, pp. 1-8.
- [4] Singh, Manjit, et al. "Anti-inflammatory activity of aqueous extract of *Mirabilis jalapa* Linn. leaves." *Pharmacognosy Research*, Vol. 2, No. 6, 2010, pp. 364-67.
- [5] Ravi Kanth, V., and P. V. Diwan. "Analgesic, antiinflammatory and hypoglycaemic activities of *Sida cordifolia*." *Phytotherapy Research: An International Journal Devoted to Pharmacological and Toxicological Evaluation of Natural Product Derivatives*, Vol. 13, No. 1, 1999, pp. 75-77.
- [6] Ballick, M., and P. Cox. "Plants, people and culture: the science of ethnobotany. New York." *Scientific American Library*, 1997.
- [7] Sharma, P. C., M. B. Yelne, and T. J. Dennis. *Database on medicinal plants used in Ayurveda*. Central Council of Research Ayurveda Siddha, Vol. 8, 2007, pp. 42-58.
- [8] Sutradhar, Ranajit K., et al. "Alkaloids of *Sida cordifolia* L." *Indian Journal of Chemistry*, Vol. 46, 2007, pp. 1896-1900.
- [9] Ghosal, S, et al. "Alkaloids from *Sida cordifolia*." *Phytochemistry*, Vol. 14, 1975, pp. 830-32.
- [10] Sutradhar, R. K., A. K. M. M. Rahman, and M. U. Ahmad. "Three new flavonol C-glycosides from *Sida cordifolia* Linn." *Journal of the Iranian Chemical Society*, Vol. 4, No. 2, 2007, pp. 175-81.
- [11] Sutradhar, Ranajit K., et al. "Bioactive flavones of *Sida cordifolia*." *Phytochemistry Letters*, Vol. 1, No. 4, 2008, pp. 179-82.
- [12] Kokate, CK, et al. "Practical pharmacognosy." *Vallabh Prakashan*, 2000, pp. 107-30.
- [13] Khandalwal, K. R., and V. K. Sethi. "Practical Pharmacognosy techniques and experiments." *Nirali Prakashan*, 1999, pp. 146-48.
- [14] Sambandam, Bharathi, et al. "Extraction and isolation of flavonoid quercetin from the leaves of *Trigonella foenum-graecum* and their anti-oxidant activity." *International Journal of Pharmacy and Pharmaceutical Sciences*, Vol. 7, No. 6, 2016, pp. 120-24.
- [15] de Almeida, Patricia, et al. "Anti-inflammatory activity of triterpenes isolated from *Protium paniculatum* oil-resins." *Evidence-Based Complementary and Alternative Medicine*, Vol. 2015, 2015, pp. 1-10.

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- [16] Wilches, Isabel, et al. "Evaluation of the anti-inflammatory activity of the methanolic extract from *Jungia rugosa* leaves in rodents." *Journal of Ethnopharmacology*, Vol. 173, 2015, pp. 166-71.
- [17] Tapas, Ahmad R., D. M. Sakarkar, and R. B. Kakde. "Flavonoids as nutraceuticals: A review." *Tropical Journal of Pharmaceutical Research*, Vol. 7, No. 3, 2008, pp. 1089-99.
- [18] Ghasemnezhad, Mahmood, Mohamad Sherafati, and Gholam Ali Payvast. "Variation in phenolic compounds, ascorbic acid and antioxidant activity of five colored bell pepper (*Capsicum annum*) fruits at two different harvest times." *Journal of Functional Foods*, Vol. 3, 2011, pp. 44-49.
- [19] Vinegar, R., W. Schreiber, and R. Hugo. "Biphasic development of carrageenin edema in rats." *Journal of Pharmacology and Experimental Therapeutics*, Vol. 166, 1969, pp. 96-103.
- [20] Flower, R. J., et al. "Effects of anti-inflammatory drugs on prostaglandin biosynthesis." *Nature New Biology*, Vol. 238, 1972, pp. 104-06.
- [21] Higgs, Gerald A., et al. "The effects of non-steroid anti-inflammatory drugs on leukocyte migration in carrageenin-induced inflammation." *European Journal of Pharmacology*, Vol. 66, 1980, pp. 81-6.
- [22] Castro, J., et al. "Diverse effect of SKF 52 and antioxidants on CCL4 induced changes in liver microsomal P-450 content and ethylmorphine metabolism." *Life Sciences*, Vol. 7, 1968, pp. 129-36.
- [23] Della Loggia, Roberto, et al. "The role of flavonoids in the anti-inflammatory activity of *Chamomilla recutita*." *Clinical and Biological Research*, Vol. 213, 1968, pp. 481-86.
- [24] Vasudevan, Mani, Kumar Kishore Gunnam, and Milind Parle. "Antinociceptive and anti-inflammatory effects of *Thespesia populnea* bark extract." *Journal of Ethnopharmacology*, Vol. 109, No. 2, 2007, pp. 264-70.
- [25] Kim, HyunPyo, et al. "Effects of naturally occurring flavonoids on inflammatory responses and their action mechanisms." *Natural Product Sciences*, Vol. 6, No. 4, 2000, pp. 170-78.