

## QUALITY AND TOXICITY STUDY ON DEVIL'S CLAW CAPSULES MARKETED IN SAUDIA ARABIA

<sup>1</sup>Naif O. Al-Harbi, <sup>2</sup>Arif H. Shah, <sup>3</sup>Mohamed J.H. Faraj, <sup>4</sup>Nawal A. Aba-Alkhail, <sup>5</sup>Riyadh M. Al-Ashban and <sup>6</sup>Saleh A. Bahashwan

<sup>1</sup>Pharmacy Department, College of Health Sciences, King Saud University, Riyadh.<sup>2,3</sup> Saudi food and drug authority central lab, Riyadh. <sup>6</sup>Pharmacy Department, College of Health Sciences, Taibah University, Medina Mpnawarah. K.S.A

### ABSTRACT

Devil's Claw is used in osteoarthritis; rheumatoid arthritis, diabetes, indigestion and heartburn. The tuber is mostly used as remedy for gall, liver, kidney and bladder problems; but western herbalists sell them mostly in the treatment of rheumatic pain, gout and joint problems, mainly arthritis and lumbago. Devil's Claw may also be used as a lymphatic system stimulant to help detoxify the entire body. It has a cooling energy with bitter and astringent tastes, and is considered an alterative, anti-inflammatory and analgesic herb for low back pain.

Devil's claw treatment in this study showed no alarming signs and symptoms of toxicity during the current acute, sub-acute and chronic toxicity studies both in male and female mice as well as in female rats as second animal model. The significant decrease in uric acid levels ( $P < 0.01$ ) in the serum of treated animals may be attributed to some Devil's claw chemical constituents. Precautions for prolonged use of Devil's claw should be taken into consideration, so that the body uric acid levels remain within the normal range.

### INTRODUCTION

Devil's Claw (*Harpogophytum procumbens* DE Candolle) family: Pedaliaceae, is a plant with bright pinkish flowers native to south and southwestern Africa, Kalahari deserts, Namibia and Island of Madagascar. The name of Devil's Claw is derived from the herb's unusual fruits, which seem to be covered with numerous small hooks. The secondary storage roots, or tuber, of the plant is employed in herbal supplements<sup>(1)</sup>. Devil's Claw is used in osteoarthritis; rheumatoid arthritis, diabetes, indigestion and heartburn<sup>(2-4)</sup>. Also the tuber is mostly used as remedy for gall, liver, kidney and bladder problems<sup>(5-6)</sup>; but western herbalists use them mostly in the treatment of rheumatic pain, gout and joint problems, mainly arthritis and lumbago<sup>(3,5,6-8)</sup>. Devil's Claw may also be used as a lymphatic system stimulant to help detoxify the entire body<sup>(10)</sup>. It has a cooling energy with bitter and astringent tastes, and is considered an alterative, anti-inflammatory and analgesic herb for low back pain<sup>(11-14)</sup>.

Previous reports indicated that the following natural compounds were isolated from the rhizome of Devil's Claw: Iridoid glycosides: harprocumbide A, harprocumbide B, 6-O- $\alpha$ -D-

galactopyranosylharpagaside, and harpagoside, harpagide, 8-cinnamoylmyoporoside, 8-O-feruloylharpagide, procumbide, 6"-O-(p-coumaroyl)-procumbide, 8-O-(p-coumaroyl)-harpagide and 8-O-(cis-p-coumaroyl)-harpagide. In addition, Flavonoids, mainly kaempferol and luteolin glycosides, Phenolic acids; chlorogenic and cinnamic acid; harpagoquinone; diterpenes: (+)-8,11,13-totaratriene-12,13-diol and (+)-8,11,13-abietatrien-12-O1 and other miscellaneous compounds including phenylethanoid glycosides; triterpenes, sterols, oleanolic & ursolic acid derivatives, esters, caffeic acid; acteoside, isoacteoside, 6'-O-acetylacteoside; and sugars<sup>(15)</sup>.

Also, active constituents: diterpenes: (+)-8,11,13-totaratriene-12,13-diol and (+)-8,11,13-abietatrien-12-O1 isolated from Devil's claw were found to possess antiplasmodial activity, however. Iridoid glycosides represent the main active compounds of Devil's claw<sup>(15-17,20)</sup>.

The secondary tubers of the herb contain twice as much harpagoside as the primary tubers. As such, these secondary tubers contain the preferable concentration of active ingredients<sup>(18)</sup>. Harpagoside and other iridoid glycosides found in the plant may be responsible for the herb's anti-inflammatory and analgesic actions<sup>(2,13,19)</sup>.

In Europe, doctors treat some conditions, like, arthritis with an injection of devil's claw extract and in treating people suffering from low back pain or arthrosis of hip or knee (11,16,20-21)

## MATERIALS AND METHODS

### Sampling

The drug samples were withdrawn from all the specified storage conditions and were subjected to physical, chemical and microbiological analysis. The samples were collected with an interval of 6 months, starting from Zero time till the end of shelf life of the product. Samples were analyzed for the presence of any toxic heavy metal, pesticides residue, and mycotoxins. Samples were subjected to acute, sub-acute, and chronic toxicity studies. During acute and sub-acute toxicity studies two animal models comprising of: (i) male and female mice, and (ii) female rats were used. Chronic toxicity studies were conducted only in male and female mice.

### Stability studies

#### Physical Tests

##### Determination of density:

The test was carried out according to the official method as follows: British Pharmacopoeia 2002, Appendix-VG A175.

##### Determination of Specific gravity

The test was performed according to the following official method: United States Pharmacopoeia, USP25, Chapter 841.

##### Determination of Refractive Index:

The test was conducted according to the following official method: European pharmacopoeia method 2.2.6. using universal refractometer, (Abbe type) Dual scale model, ranges nD 1.30 to 1.70:0.001 (estimation to 0.0001), and 0 to 95: 0.5% sugar by weight.

##### Disintegration time of capsules:

The disintegration test determine whether capsules disintegrate within the prescribed time when placed in a liquid medium under the experimental conditions given by United States Pharmacopoeia and National Formulary (22) (Nutritional Supplements Official

Monographs, Disintegration and Dissolution of Nutritional Supplements).

##### Loss on drying:

Loss on drying is the loss of mass expressed as percent (m/m). It is carried out by placing the manufacturer's described quantity of the sample in a weighing watch glass previously dried under the conditions prescribed for the drug to be examined.

The sample was dried for 3 hours in oven at  $100^{\circ}\text{C} \pm 5^{\circ}\text{C}$ . After cooling, the weight of the watch glass with the sample was recorded and the loss on drying was determined.

##### Potentiometric determination (pH):

The pH was measured at the time of testing, by direct inserting the electrode of previously calibrated pH meter (Microprocessor pH 211 HANNA Instruments) into the sample which was prepared according to the conditions described for the drug under examination.

##### Chemical analysis:

All chemical tests and assays were carried out according to the manufacturer's files and/or the methods specified in ref<sup>(23)</sup>.

##### Elemental analysis:

Accurately weighed 1 g of the sample was transferred to an ashing crucible, it was then placed inside a muffle furnace till ashing was completed. The ash was dissolved in 10 ml of 50% aqueous solution of nitric acid with slight heating on a small flame. The contents of the crucible were filtered through micro membrane filter into a 100 ml volumetric flask. The crucible was washed with distilled water and the washing was transferred into the same flask and the volume was completed with distilled water and mixed well. The concentrations of different elements in the solution were determined by using GBC-906 atomic absorption spectrophotometer. The level of each element was calculated by using previously plotted calibration curve and recorded as ppm ( $\mu\text{g/g}$ ) on dry weight of the examined samples<sup>(24)</sup>.

#### *Specific tests:*

Assays of some of the active components in the drug products under current investigation were performed following the procedure given in the registration files of the products or following the official protocol<sup>(23)</sup>.

#### *Detection of Pesticides Residue:*

The drugs were tested for the pesticides residues. Different isomers were also checked: DDT, BHC, Lindan, Heptachlor, Methoxychlor, Chlorolane, Toxaphene, Endosulfan, TDE, Dieldrin and Endrin as described<sup>(24-28)</sup>.

#### *Aflatoxins Determination:*

The drug in the present study, was tested in duplicate for the aflatoxins. A quantitative evaluation of aflatoxin were carried out through antigen antibody reaction using ELISA (Enzyme linked immunosorbent assay) technique on minilyser (fully automated system), modified Tecan RSP 5051 by Tecan company using RIDASCREEN and toxin total screening kit (Art. No. 470), manufactured by R-Biopharm AG, Darmstadt, Germany.

#### *Type of toxicity:*

The toxicity studies were performed on the drugs according to Loomis<sup>(29)</sup>, WHO Technical Report No. 872 (1998), and Eu. P. 3<sup>rd</sup> Edition method 2.6.9. Animals were observed for any abnormal signs during the acute, sub-acute, and chronic toxicity treatments in male and female mice; and female rats. The animals were observed at: 5, 15, and 30 min., 1, 2, and 4 hours on day 1; then once a day throughout the observation period. The results were evaluated by comparing the treated with the control one. Animals died within the first 24 hrs were discarded.

#### *Design of study and experimental animals*

The study was conducted on laboratory bred Swiss albino mice. In each of the toxicity treatments, sixty mice (30 male and 30 female mice kept separately) were randomly assigned to the control and treatment groups. Animals were chosen to be between 6-7 weeks of age and body weight ranged from 18-22 g. Mice

were kept in the standard laboratory conditions (12 hrs dark/12 hrs light cycle) as regards their feeding, lighting, temperature, humidity, etc., and not more than five animals per cage.

For using different animal model to study the acute and sub-acute toxicity, Sprague- Dawley female rats were selected as a second animal model. Ten female rats were used for each product and for control during this study. In order to eliminate the sex variation, only female rats were used throughout the acute and sub-acute toxicity studies.

The drug products under study were dispersed in 0.1% CMC (carboxy methyl cellulose) solution. The prepared fluids were delivered orally using high dose (acute), repeated dose toxicity levels (sub-acute) and recommended repeated dose (chronic) for six months. As the body weight and distilled water intake increased by time, the daily dose was adjusted weekly compared to the initial dose. Accordingly, each animal received the right dose during the chronic study period. The daily dose was calculated from the therapeutic dose specified by the manufacturers. The control group animals received only 0.1% CMC in the same dose. The food supply for the experimental animals was from: Grain Soils and Flour Mills Organization, Riyadh Branch.

The acute, sub-acute, and chronic toxicity studies were performed using the recommended feeding needles (sea & tube style constructed of stainless steel tubing and balls, 20 mm gauge, 25 mm length and 2.2 mm ball diameter for mice and 18 mm 76 mm length and 2.25 mm ball diameter for rats).

#### *Statistical analysis*

The data were expressed as mean  $\pm$  SEM. Student's t-test was used to determine the statistical significance of data.  $P < 0.05$  was regarded as significant;  $P < 0.01$  highly significant, and  $P > 0.05$  as non-significant.

#### **RESULTS AND DISCUSSION**

Devil's claw (*Harpogophytum procumbens*) capsules were stored under different storage conditions for twelve months and samples were withdrawn for

analysis according to specified time intervals. There were no changes in the physical properties of the capsules after six months of storage under specified conditions. Nevertheless, samples stored under "CH1" and "CH2" conditions for twelve months became fragile and the contents of the Devil's capsule, changed to brown colored lump with intense smell. These changes do not comply with the normal characters given for the capsule and its contents in the specifications (Table 1).

As regards the loss on drying and disintegration time of the samples exposed to different conditions is concerned, no significant changes were observed after six months of storage. All these samples complied with the given specifications. As regards the percentage of loss on drying is concerned, it increased from 4.8% at zero time to, 6.4% and 8.3% after 12 months of storage under "CH1" and "CH2" conditions respectively. From these results, a direct relationship between the storage conditions (temperature and humidity) and changes in physical properties of the examined product can be observed.

It is worth mentioning that harpagoside contents were more than the given specification limits in the samples tested at zero time. The harpagoside contents of samples stored at different storage conditions decreased gradually during the storage periods and remained within the given range (Table 1).

The microbiological analysis of the product under different storage conditions during the study period revealed that all tested samples were free from pathogen markers and the total viable counts for bacteria and fungi were within the limits given in the specifications of the product. These results showed the physical and microbiological stability of the drug product.

Concerning the elemental analysis, Devil's capsules showed high contents of sodium, potassium, calcium and magnesium while other elements including some toxic heavy metals in the analysis list, could not be found, indicating the drug to be devoid of the tested heavy metal toxicity.

The samples were tested for the existence of mycotoxin contents that were found to be within the acceptable international limits. Furthermore, no pesticides residues could be detected.

During oral toxicity studies with Devil's claw, the animals in the treatment groups did not show any abnormal signs of toxicity as compared to the control groups; and all animals survived through out the study period. Results of the toxicity studies on Devil's claw revealed that there was a similar weight gain both in animals in the treatment groups and control groups. The results on body weight of animals are tabulated in Table 2.

It is believed that Devil's claw may be used as a lymphatic system stimulant which helps to detoxify the entire body<sup>(10)</sup>. Furthermore, the effect on the digestive system of animals in the treatment groups is the second major area of Devil's claw use. It is reported that Devil's claw is used as a tonic and cure indigestion and heartburn<sup>(4)</sup>. Absorption of nutrients from all the gut is improved and from that the body begins to be better nourished at all levels. The bitter taste is vital for this action, which improves the function of the liver in absorption of nutrients and in cleaning and detoxifying the body. The gall bladder is stimulated to release bile so that conditions such as indigestion and constipation are relieved. These facts may be the reason for increase in the body weight and healthy look of the animals in the treatment groups. The effect of Devil's claw on the average organs weights (weight per 100 g body weight) in all the treatment groups showed no significant effects as compared to the control groups (Table 3). Mice and rats in acute and sub-acute toxicity studies during gross examination showed all vital organs to maintain normal organ texture with no obvious signs of abnormal toxicity. The histopathological results confirmed all the examined organs and bone marrow to be similar and normal and comparable to the animals in the respective control groups.



Table 2: The effect of different dose treatments with Devil's claw capsules on water intake &amp; body weight of tested animals.

Indices	Treatment	Animal group	Male Mice			Female Mice			Female Rat		
			Acute	Sub acute	Chronic	Acute	Sub acute	Chronic	Acute	Sub acute	
Body weight/gm	Before	Control	20.4±1.4	20.5±1.0	20.2±0.8	19.8±0.7	20.4±0.7	20.6±0.9	259±6.5	258±4.5	
		Treated	20.5±1.3	20.1±0.8	20.4±1.2	19.8±1.3	19.5±0.6	20.1±0.9	262±8.0	263±8.0	
	After	Control	22.9±1.2	24.7±0.8	39.0±1.2**	21.9±1.0	24.2±0.6	36.3±0.9**	265±6.5	274±5.0*	
		Treated	22.8±1.0	24.8±0.7	38.2±1.1**	22.3±1.1	23.6±0.6	34.5±0.8**	267±8.0	274±8.0*	
	Water intake/ml	Before	Control	NR	NR	3.9±0.1	NR	NR	3.8±0.1	NR	NR
			Treated	NR	NR	3.9±0.1	NR	NR	3.7±0.1	NR	NR
		After	Control	NR	NR	5.6±0.1	NR	NR	4.8±0.1	NR	NR
			Treated	NR	NR	5.6±0.1	NR	NR	4.7±0.1	NR	NR

Results are expressed as mean ± SEM.

P&gt;0.05: (non-significant), \*P&lt;0.05: (Significant), \*\*P&lt;0.01: (highly Significant), compared with the control groups using paired student's t-test.

NR = Not required.

Table 3: The effect of different dose treatments with Devil's claw capsules on the average weight of vital organs/ 100g body weight of tested animals.

Organ	Animal group	Male Mice			Female Mice			Female Rat	
		Acute	Sub acute	Chronic	Acute	Sub acute	Chronic	Acute	Sub acute
Heart	Control	0.71±0.01	0.71±0.01	0.80±0.01	0.70±0.01		0.75±0.01	1.1±0.07	
	Treated	0.71±0.01	0.71±0.01	0.79±0.01	0.69±0.01	0.69±0.01	0.73±0.01	1.1±0.10	1.0±0.01
Lungs	Control	0.92±0.02		1.60±0.10	0.91±0.02		1.30±0.10	1.94±0.08	
	Treated	0.90±0.01	0.90±0.01	1.60±0.10	0.90±0.01	0.90±0.01	1.30±0.10	1.89±0.010	1.98±0.02
Liver	Control	6.1±0.1		8.7±0.2	5.7±0.1		7.5±0.2	8.3±0.2	
	Treated	5.9±0.1	6.0±0.1	8.6±0.2	5.7±0.1	5.7±0.1	7.3±0.1	8.2±0.1	8.2±0.1
Kidneys	Control	1.21±0.02		2.70±0.10	1.21±0.02		2.17±0.05	2.0±0.06	
	Treated	1.20±0.07	1.21±0.02	2.50±0.14	1.21±0.01	1.21±0.01	2.22±0.06	1.97±0.04	2.0±0.02
Spleen	Control	0.55±0.01		0.75±0.02	0.55±0.01		0.72±0.01	0.57±0.02	
	Treated	0.55±0.01	0.55±0.02	0.75±0.01	0.54±0.01	0.54±0.02	0.7±0.01	0.56±0.01	0.57±0.01
Testes	Control	0.77±0.01	0.77±0.01	1.35±0.06	NR	NR	NR	NR	NR
	Treated	0.77±0.01	0.77±0.01	1.40±0.15	NR	NR	NR	NR	NR
Ari- aries	Control	NR	NR	NR	0.11±0.01		0.12±0.01	0.78±0.02	
	Treated	NR	NR	NR	0.10±0.006	0.10±0.006	0.12±0.004	0.78±0.02	0.78±0.02

Results are expressed as mean ± SEM.  
P>0.05: (non-significant), \*P<0.05: (Significant), \*\*P<0.01: (highly Significant), compared with the control groups using paired student's t-test.  
NR = not required.

**Table 4: Biochemical & Hematological indices of tested animals after different dose treatments with Devil's claw capsules.**

Indices	Male Mice				Female Mice				Female Rat		
	Control	Acute	Sub acute	Chronic	Control	Acute	Sub acute	Chronic	Control	Acute	Sub acute
<b>Biochemical</b>											
Glucose Mmol/l	5.4±0.3	5.3±0.4	5.4±0.3	5.3±0.2	5.1±0.3	5.0±0.1	5.0±0.7	5.4±0.6	6.3±0.6	6.5±0.2	6.1±0.5
Urea Mmol/l	6.1±0.4	6.1±0.3	5.9±0.4	6.4±0.2	6.0±0.3	5.9±0.2	5.9±0.3	6.2±0.8	7.5±0.3	7.6±0.3	7.3±0.8
Creatinine µmol/l	28.7±2.0	28.3±0.7	28.0±0.8	29.1±1.4	26.8±1.3	26.6±1.1	27.3±0.9	26.4±1.3	62.0±2.0	61±1.0	62.6±6.6
Uric acid µmol/l	62±6.0	42±5.0**	45±3.5**	43±3.0**	59±3.0	39±1.5**	39±1.0**	38±2.0**	118±10.0	88±9.0**	91±4.0**
Calcium Mmol/l	1.29±0.10	1.82±0.1	1.88±0.1	1.9±0.01	1.86±0.1	1.82±0.1	1.78±0.1	1.88±0.1	2.7±0.1	2.6±0.1	2.8±0.1
AST U/L	100±14.0	112±16.0	119±14.0	109±8.0	100±12.0	110±7.0	114±9.0	110±8.0	85±7.0	84±8.0	82±4.0
ALT U/L	56±7.0	61±12.0	63±5.0	56±3.0	54±7.0	63±3.0	63±14.0	56±8.0	55±5.0	56±7.0	54±5.0
ALP U/L	93±8.0	101±8.0	101±9.0	94±14.0	91±12.0	99±11.5	98±14.0	97±15.0	91±8.0	93±6.0	97±8.0
<b>Hematological</b>											
WBC X10 <sup>9</sup> /L	5.6±0.4	5.9±0.3	6.1±0.3	5.6±0.8	5.2±0.3	5.3±0.3	5.0±0.6	5.2±0.7	10.6±1.1	10.6±0.7	10.9±1.2
RBC X10 <sup>12</sup> /L	6.4±0.5	6.1±0.1	6.5±0.3	6.7±1.1	6.5±0.4	6.0±0.4	6.4±0.6	7.0±0.2	7.7±0.4	7.4±0.3	7.3±0.3
Hg g/dL	12.9±0.5	12.9±0.1	13.0±0.8	13.3±0.9	12.7±0.5	12.8±0.5	12.9±0.6	13.0±0.7	13.5±0.6	13.5±0.7	13.5±0.3
Platelets X10 <sup>9</sup> /L	503±17.0	491±23.0	508±38.0	584±96.5	485±24.0	493±13.0	458±29.0	601±87.0	630±53.0	665±48.5	634±44.0
MCV fL	51.7±1.1	51.8±2.1	53.0±3.5	52.2±1.2	51.1±0.7	51.8±2.3	51.0±1.8	52.3±2.4	55.0±1.2	55±0.6	55±1.8
HCT %	38.7±0.7	38.4±0.6	39.0±0.7	39.5±2.6	38.8±1.0	38.3±0.8	38.5±0.3	38.5±1.4	40.6±1.6	42.3±2.4	40.0±2.5

Results are expressed as mean±SEM. \*p>0.05 (non-significant). \*\*p<0.05 (significant). \*\*\*p<0.01 (highly significant), compared with the control groups using paired student's t-test.

Studies on the biochemical parameters reflected a highly significant ( $P < 0.01$ ) decrease in uric acid levels in mice after acute, sub-acute and chronic toxicity studies. Similar changes were observed in female rats included in acute and sub-acute toxicity studies<sup>(29)</sup>. The reduction in uric acid concentrations observed in all the treatment groups as compared to the control, might explain the analgesic, anti-inflammatory and anti-arthritis effects of Devil's claw. The reduction of uric acid noticed in Devils claw treatment groups during the current toxicity studies revealed gradual reduction in inflammation and the pain arising from it. These results support the earlier findings<sup>(3,5,6,9)</sup> which showed that Devil's claw harpagosides and other iridoide glycosides were responsible for the herb's anti-inflammatory, anti-arthritis and analgesic actions. Based on such properties herbalists use Devil's claw for the treatment of rheumatic pain and joint problems, mainly arthritis and lumbago. On the other hand, one study reported no evidence for anti-inflammatory activity of Devil's claw in the treatment of arthritic disease<sup>(30)</sup>. It is also worth mentioning that during current Devil's claw treatment showed no significant decrease in the cholesterol levels of animals which is contrary to the earlier reports<sup>(31-32)</sup> and warrants detailed pharmacological investigations on this aspect.

The hematological data revealed no changes in the studied parameters, in treated animals at all levels of toxicity studies (acute, sub-acute and chronic) and the results were similar and comparable the control groups (Table 4).

The biochemical studies showed reduction in uric acid levels in the animals in different treatment groups as compared to the control. Moussard<sup>(33)</sup> indicated that each allopathic anti-inflammatory medication has its own profile of side effects ranging from stomach disorders to serious blood abnormalities, however, none of side effects were observed in the current toxicity studies, the visceral condition of the animals in the current toxicity studies was found normal and histopathological studies revealed no serious side

effects of Devil's claw treatment. All the vital organs were normal and comparable to the control.

The effects of Devil's claw chronic treatment on male mice fertility was also studied which revealed that the sperm count, motility and sperm viability were found comparable to the control fertile untreated male mice, which were found to be  $\geq 14 \times 10^6/\text{ml}$ ,  $\geq 50\%$ , and  $\geq 50\%$  respectively. These results clearly showed Devil's claw treatment to be devoid of spermatotoxic potential.

In conclusion, Devil's claw treatment showed no alarming signs and symptoms of toxicity during the current acute, sub-acute and chronic toxicity studies both in male and female mice as well as in female rats as second animal model. The significant decrease in uric acid levels in the serum of treated animals may be attributed to some Devil's claw chemical constituents. Such a change in uric acid seems to be beneficial in treatment of some patients suffering from hyperuricaemia. However, it should be born in mind that the role of uric acid as an important biological antioxidant play a major role in both extracellular and intracellular defense mechanisms. Therefore, precautions for prolonged use of Devil's claw should be taken into consideration, so that the body uric acid levels remain within the normal range. Furthermore, the aspect of possible 'drug-herb' interaction should be addressed.

#### REFERENCES

1. Tyler, L. Herbal Secrets of Rainforest Tropical Plant Database, Prima Publishing, Rockline, CA. (1998)
2. Mahomed, I.M. and Ojewole, J.A., *Phytother Res.*, 18(12):982-989, (2004).
3. Ody, P., *The Complete Medicinal Herbal*, Dorling Kindersley, New York. P. 110. (1993).
4. Weiss, R.F., *Herbal Medicine*, Gothenburg, Sweden: AB Arcanum, 238-239. (1988)
5. Pahlow, M. and Das, *Grosse Buch der Heilpflanzen*, Graefer und Unser, Munich, Germany. pp. 423-424(1993).

6. Mabey, R., *The New Age Herbalist*, Macmillan Publishing Co. New York. P. 96(1988).
7. Gagnier, J.J., Chrubasik, S. and Manheimer, E., *BMC Complement Altern. Med.* 15(4): 13(2004).
8. DerMarderosian, A. and Beutler, J.A. *The Review of Natural Products. The Most Complete Source of Natural Product Information, Facts and Comparisons.* 111 West Port Plaza, Suite 300 St. Louis, Missouri 63146-3098. pp. 144-145; 181-182; 212-213; 264; 500; 660-661(2002).
9. Chrubasik, S., Traditional herbal therapy for the treatment of rheumatic pain: preparations from devil's claw and stinging nettle. Department of Pharmaceutical Biology, University of Heidelberg. [Chrubasik, S. (1996). *Phytotherapy*, 3:1] (1997).
10. Argus, J., *Improving The Lymph System.* Rensselaerville. New York(2000).
11. Gagnier J.J., van Tulder, M.W., Berman, B. and Bombardier, C., *Spine*, 32(1):82-920 (2007).
12. Huang, T.H., Tran, V.H., Duke, R.K., Tan, S., Chrubasik, S., Roufogalis, B.D. and Duke, C.C., *J. Ethnopharmacology*, 104 (1-2):149-155(2006).
13. Chrubasik, S. *Orthopade*. 33(7):804-808(2004).
14. Frawley, D. and Lad, V., *The Yoga Of Herbs.* Lotus Press, Twin Lakes. WI. P. 200(1986).
15. Boje, K., Lechtenberg, M. and Nahrstedt A., *Planta Med.* 69(9):820-825(2003).
16. Qi, J., Chen, J.J., Cheng, Z.H., Zhou, J.H., Yu, B.Y. and Qiu, S.X., *Phytochemistry* 67(13):1372-1377(2006).
17. Clarkson, C., Campbell, W.E. and Smith, P.J., *Planta Med.* (2003). 69(8):720-724.
18. Leung, A.Y. and Foster, S., *Encyclopedia Of Natural Ingredients Used In Food, Drugs And Cosmetics 2<sup>nd</sup> Ed.* John Wiley & Sons. New York. Wiley-Interscience Publication. pp. 208-210(1986).
19. Andersen, M.L., Santos, E.H., Seabra-Mde, L., Da-Silva, A.A. and Tufik, S. *J. Ethnopharmacology* 91(2-3):325-330(2004).
20. Clarkson, C., Staerk, D., Hansen, S.H., Smith, P.J. and Jaroszewski, J.W., *J. Nat. Prod.* 69(9):1280-1288(2006).
21. Wagener, T. and Lupke, N.P., *Phytotherapy Res.* 17(10):1165-1172(2003).
22. *United States Pharmacopeia and National Formulary, United States Pharmacopoeial Convention Inc., Rockville, MD, USA, 25<sup>th</sup> Ed.*(2002).
23. *European Pharmacopoeia 3<sup>rd</sup> Edition.* 2.6.9(1997).
24. Khan, I.A., Allgood, J., Walker, L.A., Abourashed, E.A., Schlenk, D. and Benson, W.H., *J. AOAC International* 84(3):936-939(2001).
25. Lino, C.M., Guarda, L.M.C. and Silveira, M.I.N. Portugal., *J. AOAC International* 82 (5): 1206-1213(1999).
26. Yoon, H.R., Cho, S.Y., Kim, J.M., Yoon, I.B., Park, M.K. and Park, J.H., *Chromatographia* 49 (9-10): 525-534(1999).
27. Veningerova, M., Prachar, V., Kovacicova, J. and Uhnak, J., *J. Chromatogr. A* 77 (1-2): 333-347(1997).
28. Kurpios, M. and Barylo, L., *Gamma-HCH. Chem. Anal. (Warsaw)* 27(5-6):487-490(1982).
29. Loomis, *Essentials of Toxicology (Third ed.)*, Lea and Febiger, Philadelphia, USA, p. 241(1978).
30. Whitehouse, L.W., Zenamirouska, M. and Paul, C.J. *Can. Med. Assoc. J.* 129 (3): 249-251(1983).
31. Zimmerman, W., *Rehab. U. Physical Med.* 18 (1977).
32. Betterbodz.com: [http://www.betterbodz.com/library/devils\\_claw.html](http://www.betterbodz.com/library/devils_claw.html).
33. Moussard, C., Alber, D. and Toubin, M.M. *Essent. Fatty acids.* 46:283-286 (1992).

#### ACKNOWLEDGMENT

Acknowledgment and extreme gratefulness of the principle and Co investigators to King Abdulaziz City for science and technology, General Directorate of Research Grants Programs, for its generous grant and continuous support.

## دراسة على جودة وسمية كبسولات نبات مخلب الشيطان المسوقه في المملكة العربية السعوديه

<sup>1</sup>تايف عبيد الحربي ، <sup>2</sup>عارف حسين شاه ، <sup>3</sup>محمد جمال الدين حامد فرج ، <sup>4</sup>نوال عبدالله أبا الخليل ، <sup>5</sup>رياض محمد العشبان ، <sup>6</sup>صالح عبدالرحمن باحشوان

<sup>1</sup> قسم الصيدلة-كلية العلوم الصحية-جامعة الملك سعود، الرياض. <sup>2-5</sup> هيئة الدواء والغذاء- المختبر المركزي، الرياض. <sup>6</sup> قسم الصيدلة- كلية العلوم الصحية-جامعة طيبة، المدينة المنورة- المملكة العربية السعودية.

### الملخص

يستخدم نبات مخلب الشيطان في علاج التهاب المفاصل والروماتويد ومرض السكري وعسر الهضم وحرقان المعدة ، وتستخدم الدرنات في علاج مشاكل المرارة والكبد والكلية والمثانة. ولكن علماء الأعشاب الغربيين استخدموه في علاج الآلام الروماتيزمية والنقرس وآلام المفاصل والفقرات القطنية كما استخدم أيضا كمدنز للجهاز الليمفاوي ليساعد على معادلة سمية الأجسام الغريبة ولهذا العشب له طعم قابض ويستخدم كمضاد للإلتهاب ومسكن لآلام الظهر.

وقد استخدمت كبسولات نبات مخلب الشيطان في هذه الدراسة بجرعات حادة وتحت الحادة و زممنة وفي جميع الأحوال لم تظهر أى علامات سمية على ذكور أو إناث الفئران البيضاء أو إناث الجرذان.

وقد حدث إنخفاض ملحوظ في مستوى حمض البوليك في الدم ، وهذا قد يرجع إلى التركيب الكيميائي لهذا النبات ، وهذا التأثير قد يكون مفيد للمرضى الذين يعانون من ارتفاع حمض البوليك في الدم ، ولكن من ناحية أخرى فإن كون حمض البوليك عامل مضاد للأكسدة ويلعب دور هام في عملية الدفاع داخل وخارج الخلية ، لذا يجب الإحتياط و عدم الإفراط في تناول كبسولات مستخلص نبات مخلب الشيطان ليبقى مستوى حمض البوليك في الدم في مستواه الطبيعي.