

Effect of Topical Cidir leaves Extract in Reducing Skin Sensitivity in Atopic Patients

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Abstract:

Objective: To determine the changes of Cutaneous sensations that occur after local application of cidir leaves extract in atopic patients and healthy individuals.

Methods: Thirty normal individuals and 30 patients with atopic dermatitis participated in the study. The study was conducted in Najaf Teaching Hospital-Najaf in the period between October 2002 and March 2004. The square wave electrical stimulator was used to stimulate fixed spots on the volar aspect of the right forearm before and after the application of cidir leaves extract. The stimulus was increased gradually and the type of cutaneous sensation that occurred was reported.

Results: Cidir leaves extract decrease the skin sensitivity both in normal and effectively in atopic patients. The mean stimulus required to induce each one of cutaneous sensation (tingling, pricking, itching and pain) was higher after the application of the cidir leaves extract. The Cutaneous sensation on other hand that induced by the stimulus was milder than before application of the extract.

Conclusion: Cidir leaves extract decrease skin sensitivity both in atopic patients and healthy individuals so it can be used as a cooling agent in cases of eczema and pruritus.

Introduction:

The genus *Zizyphus* belongs to family (Rhamnaceae). It is a genus of about 100 species of deciduous or evergreen trees and shrubs distributed in the tropical and subtropical regions of the world. *Zizyphus spina-christi*, the Arabs call it Nabka or cidir [1].

The main constituents of the cidir essential oil were alpha-terpineol (16.4%) and linalool (11.5%). The main neutral hydrocarbons were n-pentacosane forms (81%). Methyl esters isolated from leaves included methyl palmitate, methyl stearate and methyl myristate. beta-Sitosterol, oleanolic acid and maslinic acid were the main aglycones of the glycosides present in leaves. Sugars present in leaves included lactose, glucose, galactose, arabinose, xylose and rhamnose.[2]

The plant also contains four saponin glycosides [3]. The highest flavonoid content was found in the leaves (0.66%). [4]. The composition of the plant has always proved complex in its chemistry, in addition to the known alkaloids, zizyphine-F, jubanine-A and amphibine-H, a new peptide alkaloid spinanine-A has been isolated from the stem bark of *Zizyphus spina-christi*. Spinanine-A is a 14-membered cyclopeptide alkaloid of the amphibine-B type [5].

Zizyphus spina-christi has been shown to have activity against bacteria and fungi [6] and also other pathogens that are normally quite resistant. *Zizyphus spina-christi* was shown to reduce oxidative degradation[7].

The berries are tonic and will revive a failing appetite. They are also laxative and have been used as a vermifuge. It refreshes and restores, improves memory and is a remedy for high blood pressure [8]

Hypoglycemic and antihyperglycemic effects of *Zizyphus spina-christi* has been demonstrated [9].

The chemical constituents confirm the fruit's beneficial use as a tonic (table 1). The seeds were rich in protein and the leaves in calcium, iron and magnesium. The food from this plant is an important source of energy, protein and minerals[2].

The plant is already used in many parts of the world for the care of the skin. The chemical composition and phytochemicals present in the plant would suggest and substantiate the ethnobotanical and cultural reliance on this plant. [10].

TABLE 1: THE NUTRITIONAL COMPOUNDS IN ZIZYPHUS SPINA-CHRISTI.			
Chemical composition per 100 g fruit, dried			
Alanine	3.4 g	Lysine	2.3 g
Arginine	3.4 g	Magnesium	0.12 g (dry)
Ash (insoluble)	4.4 g (dry)	Manganese	13 mg/kg (dry)
Aspartic acid	15.1 g	Methionine	0.4 g
Calcium	0.61 g (dry)	Na	0.01 g (dry)
Starch	21.8 g (dry)	Phenylalaine	2.2 g
Copper	5 mg/kg (dry)	Potassium	0.13 g (dry)
Cysteine	0.5 g	Proline	5.3 g
D-fructose	16.0 g (dry)	Protein (crude)	4.8-5.6 g (dry)
D-glucose	9.6 g (dry)	Serine	3.9 g
Fat	0.9 g [2.1 g (dry)]	Sucrose	21.8 g (dry)
Fe	3.0 mg	Sulphur	0.04 g (dry)
Fibre (crude) (dry)	4.1 g (dry)	Threonine	2.2 g
Glutamic acid	17.6 g	Tyrosine	1.8 g
Glycine	3.1 g	Valine	3.1 g
Histidine	0.9 g	Vitamin B1	0.04 mg
Iron	20 mg/kg (dry)	Vitamin B2	0.13 mg
Isoleucine	2.3 g	Vitamin C	30 mg
K	1.91 g (dry)	Zinc	9 mg/kg (dry)
Leucine	3.9 g		

Lipid peroxidation plays an important role in the generation of problem skin and scalp conditions by involving changes in the sebum composition leading to increases in the immune reaction of the skin. Peroxidation and other oxidative breakdowns can be caused by environmental challenges that generate free radicals (such as exhaust pollution, industrial fumes, ozone, UV light, cigarette smoke, etc.) and by biological challenges such as micro-organisms and other detrimental conditions. An 10% *Zizyphus spina-christi* extract reduced lipid peroxidation by 66%. [11]

Atopic dermatitis (AD) is a chronic, highly pruritic, eczematous skin disease that follows patients from early childhood into puberty and sometimes adulthood. Also referred to as eczematous dermatitis, the disease often has a remitting/flaring course, which may be exacerbated by social, environmental, and biological triggers. [12]

Patients and methods:

The study was performed in the Medical Teaching Hospital-Najaf on 30 normal individuals and 30 patients with atopic dermatitis. Their ages and sexes are illustrated on (table 2).

The cidir leaves were dried, crushed and immersed in water for 24 hours.. The extract was taken and applied on fixed points in the right forearm of each of normal persons as a control and atopic patients and left for five minutes.

The measurement was performed by using a square wave electrical stimulator which is a non invasive technique to study the skin sensitivity. The positive electrode was a tungsten wire with a tip of 38 micrometers. While the negative electrode indifferent electrode consisted of a metal disc of 2 centimeters diameter covered with cotton gauze soaked with tap water. This electrode was applied to the abdomen. The pulse width was kept constant at 5 milliseconds while the pulse rate was fixed at 20 pulses per second. The positive electrode applied on each of the four spots which were selected on the volar aspect of each individual i.e. normal and atopic person. The voltage of the stimulator was increased gradually until the patient feels the stimulus as one type of skin sensations –tingling, pricking, itching or pain- which was recorded as the threshold voltage. The voltage was increased gradually until reaching a stimulus that can induce a second sensation , this stimulus called post threshold stimulus and the response recorded as second cutaneous sensation.

Results:

The cutaneous electrical threshold was lower in atopic individuals compared to healthy controls before and after the application of cidir leaves extract (table-2). This was statistically significant ($p < 0.05$). The mean post electrical cutaneous threshold was lower in atopic patients compared to normal individuals before and after cidir leaves extract application.

After the application of cidir leaves extract, the mean post electrical cutaneous threshold was increased in both normal and atopic patients. The effectiveness of the cidir leaves extract in reducing the cutaneous sensitivity was more pronounced in atopic patients than normal individuals (table-3). This was statistically significant ($p < 0.05$).

The type of cutaneous sensations induced by skin stimulation with a square wave electrical stimulator was reported. The sensations were more irritable (pricking , itching, pain) in atopic patients than normal individuals. These sensations were changed after cidir leaves extract application and become less irritable both in atopic patients and control (table-4).

Table 1: Age and sex of healthy control individuals and atopic patients.

	Control	Atopic patients
Number	30	30
Age	25± 30	20±18
Sex	20 males, 10 females	18 males, 12 females

Table 2: The mean post cutaneous electrical threshold in volts in healthy control individuals and atopic patients before and after the application of cidir leaves extract.

samples	Before application	After application	P value
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control	2.22±0.13	3.54±1.12	<0.05
Atopic patients	1.12±0.23	2.44±0.16	<0.05

(10)

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Table 3: The mean post cutaneous electrical threshold in volts in healthy control individuals and atopic patients before and after the application of cidir leaves extract.

	Before the application	After the application	P value
control	3.25±0.34	5.12±2.11	<0.05
Atopic patients	1.45±0.22	3.45±1.02	<0.05

Table 4: Cutaneous sensations before and after cidir leaves extracts application both in normal and atopic patients

	Normal individual		Atopic patients	
	Before	After	Before	After
Tingling	14	18	10	14
Pricking	12	8	10	12
Itching	4	3	6	4
Pain	2	1	4	2

Discussion:

Atopic dermatitis is an immediate (type I) hypersensitivity reaction similar to that of allergic rhinitis, bronchial asthma, atopic dermatitis, and food allergy. Although not all patients who have atopic dermatitis are atopic (a misnomer of the disease), the correlation is high, around 80%, and patients with AD often manifest other atopic diseases.[12]

Atopic patients are extremely sensitive to temperature changes, dry air exacerbates the disease. Contact with solvents, detergents, deodorants, cosmetics, and soaps can exacerbate the disease. Cigarette smoke has also provoked inflammation.[13]

Comparing atopic patients skin with that of a normal control by measuring cutaneous threshold, post cutaneous threshold and skin sensations with a square wave electrical stimulator. The cutaneous threshold was lower in atopic patients before and after using cidir leaves extract. This result was mentioned in other study.[14]

The post cutaneous threshold readings were also lower in atopic patients than control before and after cidir leaves extract application. This demonstrate statically that atopic patients skin is more sensitive to irritations as mentioned by others.[15]

After using cidir leaves extract on the skin the post threshold reading were higher than before application, this demonstrate that cidir leaves extract has cooling effect on normal and atopic persons with more efficacy in atopic patients. This result agree with what mentioned in other literatures in that, application of a 10% aqueous extract *Zizyphus spina-christi* powder. on UV-irradiated skin showed a reduction in the skin reddening.[16]

Cutaneous sensations that occurs following skin stimulations was more painful in atopic patients than control. These sensations were become less irritable after cidir leaves extract application.

This result give other indication that cidir leaves extract has cooling effect and can be used to reduce the skin sensitivity in atopic patients and may be in other pruritic skin diseases. Study by others show that aqueous leaf extract of *Zizyphus spina-christi* may possess antinociceptive properties in the rat and have a calming effect on the central nervous system. [11].

(11)

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