

# The effect of Khat (*Catha edulis*) on acute cerebral infarction

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## ABSTRACT

**Objectives:** The aim of this study was to show the effects of Khat on acute cerebral infarction (ACI), specifically regarding blood pressure, age and gender, and to open the door for further neurological research.

**Methods:** We collected 358 patients with ACI, and 335 volunteers from Al-Thowra Modern General Hospital in Sana'a, Yemen, and Thamar General Hospital, Thamar City, approximately 100 km south of Sana'a. During a one year period, from February 2003 to March 2004, we conducted research regarding blood pressure, age, and gender related to the chewing or not chewing of Khat. We conducted a comparison between the ACI group and the volunteer group, using the SPSS 10.0 Chi-square statistical methods.

**Results:** Results show that Khat increases blood

pressure in patients with ACI. The gender-related effects show that Khat affects a greater percentage of males (74.6%) compared to females (25.4%), Khat chewers in the patient group showed a statistical significance of  $p < 0.001$ . The 358 ACI patients had a mean age of 51.5 years old, while in the 335 normal individuals the mean age was 42.5 years old, showing a statistical significance of  $p < 0.001$ .

**Conclusion:** Khat is a risk to blood pressure in ACI patients, with a statistical significance of  $p < 0.001$ . Khat affects males more than females, and Khat chewers are more affected than non-chewers with a statistical significance of  $p < 0.01$ . Khat also shows a significant relationship with age, affecting older persons ( $p < 0.001$ ).

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**K**hat (*Catha edulis*) is an evergreen tree or large shrub with glabrous leaves that belong to the family *Celastraceae*. The young buds and fresh leaves of Khat, also known as Kat or Qat, are consumed by chewing. Khat originated in Ethiopia, and after discovery of its use spread to Kenya, Nyasaland (now Malawi) Uganda, Tanganyika (now Tanzania), Arabia, the Congo, Rhodesia (now Zimbabwe and Zambia), South Africa, and Somalia, exported to United States of America, and the United Kingdom.<sup>1-3</sup> Khat was used in Yemen earlier than coffee and it is immensely popular. The main effect of Khat is an increase of energy and alertness. This effect is supposedly attributable to the phenylalkylamine constituent, cathinone,<sup>1</sup> which is

the active ingredient of Khat, and it shows that the alkaloid also has an amphetamine-like effect on human beings.<sup>4</sup> The mucosa of the oral activity is considered to be the first absorption segment, thus the pharmacokinetic of the Khat alkaloid in humans explains why chewing is the preferred form of Khat ingestion. The evidence for amphetamine like stimulatory effects of Khat leaves were closely similar to those observed after cathinone 0.5 mg/kg body weight, although peak plasma concentration of cathinone after Khat was delayed.<sup>1</sup> The fact that cathinone has a close structural similarity with amphetamine, and they both share pharmacodynamic features, lead to the conclusion that cathinone is the most important active

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ingredient of Khat causing the major pharmacological effects.<sup>2</sup> Experimental work shows that cathinone is structurally related to amphetamine, and similarly increases the level of dopamine in the brain by acting on the catecholaminergic synapse. Hence, the psychostimulant effect of Khat can be accounted for by the mechanism of cathinone.<sup>5</sup> Cathinone may have cardiovascular actions similar to those of Methylenedioxymethamphetamine (MDMA), and as cocaine leads to an increased incidence of myocardial infarction, the results may have implications in terms of cardiac morbidity of amphetamine derivatives and cathinone.<sup>6</sup> The relationship between abuses of amphetamine, and its analogue "Ecstasy" and acute myocardial infarction and arrhythmias are well documented.<sup>7,8</sup> The MDMA ecstasy can lead to hypertension, epileptic seizures, and cerebral toxicity. Blood pressure and pulse rate may increase after chewing Khat.<sup>9</sup>

**Methods.** Three hundred and fifty-eight patients who suffer from ACI, and 335 controls who do not suffer from ACI, were included in the study from Al-Thowra Modern General Hospital, Sana'a City, and Thamar General Hospital, Thamar City, 100 km south of Sana'a in Yemen, from February 2003 to March 2004. Data was collected concerning age, gender, blood pressure, and chewing or non-chewing of Khat. The diagnosis of ACI was dependent upon neurological examination and a CT scan or MRI of the brain. This information was then used to study the relationship between Khat and ACI. The results were analyzed using SPSS for windows. Chi-square was used to compare the differences between the patient and control group regarding the effect of Khat on ACI, and the chewing of Khat and non-chewing of Khat in each group. In addition to the effect of Khat on blood pressure within the chewing and non-chewing of

Khat in both groups, the relationship of Khat in males and females, and the effect of Khat in relation to age group was also studied.

**Results. Effect of Khat on blood pressure (BP).** **Tables 1 & 2** show the effects of chewing and non-chewing of Khat on blood pressure in the patient and control groups. Comparison between ACI and control groups shows statistical significance in increasing BP  $p < 0.01$ .

**Relationship between Khat and gender.** **Tables 1 & 2** show the relationship between chewing and non-chewing of Khat and gender in the patient and control groups. Comparison between the ACI and control group shows that the percentage of males chewing Khat was more than females in both groups, and Khat chewing effects males more than females (**Table 3**).

**Relationship between Khat and age.** The results show a difference in the distribution of age between the 2 groups. In the ACI group, Khat chewing effects the older age groups more than the younger, however, in the control group, Khat effects the younger age group more than the older (**Tables 1 & 2**). The patients and volunteers included in this research totaled 693, the mean age of the ACI group (51.5 years old) was older, and the mean of age of normal individuals (42.5 years old), was younger as shown in **Table 4**.

**Discussion.** Khat, amphetamine and the amphetamine-derivative Ecstasy are well documented in terms of their similarities in both structure and mechanism of action.<sup>8</sup> Cathinone, the main active constituent of Khat, is a substance with an amphetamine-like action which releases endogenous catecholamine from peripheral and central neurons. The effects of Khat acts through its active ingredient, Cathinone, in which its mechanism of action is similar to amphetamine.<sup>5</sup>

Table 1 - Khat effect on blood pressure, gender, and age in the acute cerebral infarction patient group.

Variables	Chewing	Non-chewing	Total	P
<b>Blood Pressure (mm Hg)</b>				0.01
High BP	141	53	<b>194</b>	
Normal BP	99	65	<b>164</b>	
<b>Gender</b>				0.001
Male	179	63	<b>242</b>	
Female	61	55	<b>116</b>	
<b>Age (years)</b>				0.001
30-39	21	8	<b>29</b>	
40-49	47	15	<b>62</b>	
50-59	66	21	<b>87</b>	
>60	106	74	<b>180</b>	

Table 2 - Khat effect on blood pressure, gender, and age in the control group.

Variables	Chewing	Non-chewing	Total	P
<b>Blood Pressure (mm Hg)</b>				0.01
High BP	28	19	<b>47</b>	
Normal BP	101	187	<b>288</b>	
<b>Gender</b>				0.01
Male	96	118	<b>214</b>	
Female	33	88	<b>121</b>	
<b>Age (years)</b>				0.001
30-39	45	58	<b>103</b>	
40-49	42	65	<b>107</b>	
50-59	25	38	<b>63</b>	
>60	17	45	<b>62</b>	

Table 3 - Effect of Khat in relation to gender.

Gender	ACI patient group		Control group	
	Chewing	Non-chewing	Chewing	Non-chewing
Male (%)	(74.6)*	(55)	(74.4)*	(57.3)
Female (%)	(25.4)	(44.9)	(25.6)	(42.7)
		$\chi^2 = 10.097, * p < 0.001$		$\chi^2 = 16.222, * p < 0.01$

Methamphetamine has also proven to exacerbate ischemic stroke in the brain.<sup>10</sup> Amphetamine also increases blood pressure causing hypertension,<sup>11</sup> which is one of the risk factors of ACI; especially when it is increased suddenly, such as after an emotional upset, stress, anxiety due to personal, familial or other source of events or problems that may result due to increased release of catecholamine. This shows that Khat plays a role in the increase of catecholamine secretion, thus also increasing blood pressure. Amphetamines also cause myocardial infarction,<sup>12-14</sup> while coronary heart disease and cerebral stroke share major common risk factors.<sup>15</sup> Diastolic and systolic blood pressure, smoking, cardio thoracic ratio, preexisting coronary heart disease and diabetes were positively related to stroke,<sup>16</sup> also the risk of ischemic stroke is increased after acute myocardial infarction.<sup>17</sup> The relationship between amphetamine, Ecstasy, Khat and acute myocardial infarction is well-documented.<sup>7,18</sup> The effect of Khat shows statistical significance in increasing blood pressure in both ACI patients and the control group ( $p < 0.001$ ), as shown in **Table 1**. This explains the direct relationship between Khat and blood pressure, which effects Khat chewers in the patient group more than Khat chewers in the control. Therefore, this research shows that Khat plays an important role in increasing BP, thus supporting the previous studies that describe Khat's relation to increased BP and pulse rate in all volunteers studied after chewing Khat, and coincides with raised plasma cathinone concentration.<sup>19</sup> Chewing Khat in normal individuals (human volunteers) resulted in increased blood pressure and heart rate associated with an increase of cathinone plasma concentration, and this research shows significant statistical effects that Khat increases the blood pressure ( $p < 0.01$ ) as shown in **Table 1**, which may be due to Khat chewing as well as effects on functional mood disorders. This is common in most patients with ACI who have strokes suddenly after a personal or family history of anxiety or stress. Khat has an effect on increased blood pressure in both patients and normal individual groups, but the more significant effect is

Table 4 - Effect of Khat in relation to age distribution.

Age (years)	ACI patient group		Control group	
	Chewing	Non-chewing	Chewing	Non-chewing
30-39	(8.8)	(6.8)	(34.9)*	(28.2)
40-49	(19.5)	(12.7)	(32.6)*	(31.6)
50-59	(27.5)*	(17.8)	(19.4)	(18.5)
>60	(44.2)*	(62.7)	(13.2)	(21.8)
		$\chi^2 = 368.358, * p < 0.001$		$\chi^2 = 426.135, * p < 0.001$

in patients complaining of ACI as shown in **Tables 1 & 2**.

In this research, the ages of the patients and control group were divided into 30-39, 40-49, 50-59, >60 years. The results showed that the older groups are affected by Khat more than the younger age groups and Khat chewers are affected more than non chewers, and the younger ages chewing Khat are not affected so much, but this may be due to activity, exercise, nutrition and general body health and period of time of chewing Khat; in general the younger age groups are more resistant to illness than the older age groups, and the younger age groups are in better condition than the older. This is why the numbers of patients are larger in the older Khat chewing groups, as older people chewing Khat have an increased risk of ACI disease as shown in **Table 1**. The greater distribution of chewing Khat in the control group shows that the number of individuals were greater in the young age groups compared to the number of individuals in the older age group as shown in **Table 2**. However, the distribution is nearly the same in the non-chewing Khat age groups.

The distribution of Khat related to gender shows that the male patients (n=179) are more likely to chew Khat than female patients (n=61) see **Table 1**, this is why male Khat chewers are more susceptible to ACI than females. In neurological departments or files, the higher susceptibility of male ACI patients is related to females, although the males (63 non chewing patients) are less than females (55 non chewing patients) of the same patient group, showing that males still have higher statistical significance  $p < 0.001$  as shown in **Tables 1 & 3**. It could be due to the small sample collection, which was also selected randomly as in **Tables 1 & 2**. The distribution of control group shows more males than females in both chewing and non-chewing Khat groups, comparing ACI and control groups shows that Khat chewing effects males more than females with statistical significant  $p < 0.01$  as shown in **Tables 2 & 3**.

In conclusion, Khat chewing is a significant risk factor for ACI that requires further clinical study.

Khat chewing does result in increased BP, which is also proven in previous literature. Khat affects older people more than younger people, and the chewing group more than the non-chewing. Khat chewing affects males more than females, Khat chewers are affected more than non-chewers, and mainly in the patient group.

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