ORIGINAL ARTICLE

ASSOCIATION BETWEEN KHAT CHEWING AND GASTROINTESTINAL DISORDERS: A CROSS SECTIONAL STUDY

Tadele Nigussie¹, Teshome Gobena², Andualem Mossie²

ABSTRACT

BACKGROUND: Khat (Catha edulis Forsk) is a psycho-stimulant substance grown in East Africa. But its adverse effects and its prevalence are not well studied. The main aim of the present study is thus to assess the association between khat chewing and GI problems among students in Ambo University. METHODS: A cross-sectional study was conducted in January 2010 on 1005 Ambo University students. Study subjects were selected using systematic random sampling technique, and data were collected using self-administered questionnaire. Data analysis was made using SPSS version 16.0 for windows package. RESULTS: The mean age of the respondents was 20.79 ± 1.39 ranging from 18-30 years. Seven hundred twenty (71.6%) of the study participants were males and 994 (98.9%) were in the age group of 15-24 years. The prevalence of gastritis was 580 (57.7%); constipation 235 (23.4%); hemorrhoids 54 (5.4%) and that of dental problems (carries, decay, filling and extraction) was 225 (22.4%) of all study participants. Gastrointestinal disorders were found to be higher among khat chewers, where 64(36.2%)

CONCLUSION: The prevalence of gastrointestinal disorders was found to be higher among khat chewers, indicating that khat chewing could be a predisposing factor to gastrointestinal disorders. Community-based awareness creation about the adverse effect of khat use is thus recommended.

of them had dental problems; 127(71.8%) symptoms of gastritis; 86(48.6%) constipation and 26(14.7%)

KEY WORDS: Khat chewing, Gastritis, Constipation, Hemorrhoids

hemorrhoids which demonstrated statistically significant association with p < 0.001.

INTRODUCTION

Khat (Catha edulis Forsk) is an evergreen plant found commonly grown in Ethiopia, Yemen, Kenya, Sudan, Madagascar and South Africa (1). The plant is known by different names in different countries but in most of the literature it is known as Khat (2). People chew the leaves and young bud of khat for social and psychological reasons (3, 4).

The psycho-stimulant effect of khat is due to the alkaloid chemical ingredient cathinone present in the fresh leaves of the plant (*Catha edulis*) (5, 6). The chemical structure of cathinone has close resemblance to amphetamine (7, 8). The results of various in vivo and in vitro experiments indicate that cathinone could be considered as a natural amphetamine (8, 9). Cathinone enhances the releases of catecholamines from their storage areas resulting in CNS stimulation. Cathinone has also a variety of peripheral sympathomimetic activities (10, 11). The pattern of cathinone dependence is similar to that of amphetamine. Consequently, WHO has recommended that cathinone be placed under international control and it is now included in the list of controlled drugs (12, 13).

Corresponding Author: Teshome Gobena, Email:tgobena_2012@yahoo.com

¹Department of Pharmacy, Ambo University, Ambo, Ethiopia

²Department of Biomedical Sciences, Jimma University, Jimma, Ethiopia

Many people use khat for different purposes: for social recreation, to keep awake while driving long distances (14, 15), to reduce physical fatigue and to work hard for a long time (16). It is believed that students in colleges and universities commonly use khat to improve their academic performance but the fact is the opposite. The result of one study shows that the mean cumulative GPA of non-chewers was found to be significantly higher than that of chewers (17, 18).

Ethiop J Health Sci.

How could Khat chewing lead to GI disorders? In the gastrointestinal tract, the astringent characteristics of the tannins in khat accounts for periodontal disease, stomatitis, oesophagitis and gastritis (32). Tannins and cathinone contribute to constipation, the most common medical complaint of the khat user. In a randomized controlled trial, Heymann et al. 1995 (33) reported a delay in gastric emptying after chewing khat, which was attributed to the sympathomimetic action of the cathinone. Moreover, Gunaid et al. 1999 (34) found out that khat prolongs entire gut motility and Makonnen 2000 (35) reported that khat produced constipation in mice and an antispasmodic action on guinea-pig isolated ileum. The antispasmodic effect of khat extract was observed to be similar to that of damphetamine.

Khat is abundantly available in Ethiopia and is a highly valued export commodity in the country. The number of khat chewers has significantly increased in this country and khat consumption has become popular in all segments of the Ethiopian population (16, 19). Khat chewing has a positive association with gastrointestinal disorders such as dental problems, gastritis and constipation (32, 33, 34, 35). Dental problem is among the most prevalent and costly diseases affecting both developed and developing countries; yet, it is highly preventable (20, 21). Another disorder that might be associated with khat chewing is gastritis. Gastritis is inflammation of the gastric mucosa. Mild to moderate gastritis is becoming exceedingly common in the population as a whole, especially in the middle to later years of adult life (22, 23). The most common symptoms of gastritis are abdominal upset or pain, belching, abdominal bloating, nausea, and vomiting or a feeling of fullness or of burning in the upper abdomen and if severe, vomiting of blood as well as black stools may be a sign of bleeding in the stomach (24, 26). According to some researchers, constipation and hemorrhoids are also considered to have associations with khat chewing (27, 28).

According to the observation of one of the authors of this manuscript, who is working in Ambo University, khat is grown abundantly in Ambo area and many students in the university use it. Gastrointestinal problems are common complaints of students. Yet, in Ethiopia, there have been no study reports showing the association between khat chewing and gastrointestinal (GI) disorders. Therefore, the main aim of this study was to determine the association between khat chewing and GI disorders.

METHODS AND SUBJECTS

The study was conducted in Ambo University from April, 2009 to May, 2010 using a cross-sectional study design. The source population for this study was all Ambo University students and the study population was sampled students of the university. Systematic random sampling technique was employed to select samples of dormitories and cluster sampling technique was used to select study participants.

The sample size (n) was calculated by considering 97% confidence level, p = 0.5, margin error (d) 3% (0.03) and the total population size (N) of 4600. Accordingly, the estimated sample size was 1019. All voluntary students in the sampled dormitories were included in the study. Sampling was conducted through dorm to dorm survey in which, every fourth dormitory was selected through systematic random sampling and all students in a selected dormitory were included as the study participants. All volunteers in the sampled dormitories were included in the study. data collection, the drug addiction questionnaire developed by WHO (25) was used with minor modifications and certain questions pertinent to the study objectives were added. The questionnaire was translated into Amharic and distributed to all sampled students. Two trained nurses were involved in data collection, and supervision was carried out by the principal investigator.

During data collection, gastrointestinal tract disorders were identified symptomatically based on the responses of the study participants. Gastritis was defined as a pain sensation or discomfort in the upper abdomen.

Data entry, clearing and analysis were made using SPSS. To assess the association between khat chewing and gastrointestinal disorders, chi-square test and percentages were calculated. Logistic regression analysis was made to show the level of risk of gastrointestinal problems among khat chewers and non-chewers.

Ethical clearance and permission were first obtained from the Ethical Review Boards of Jimma University and then from Ambo University. The study participants were informed about the objective of the study and asked their consent to be involved in the study. Confidentiality was also maintained.

The following operational definitions were used in this study:

- Pattern: a description of frequency, duration and circumstance of khat use:
- **Previous use**: history of khat use in life time but not in the past 30 days;
- **Current use**: history of ingestion of khat in the past 30 days;
- Non-user: person who has never chewed khat in any form;
- Habitual user: frequent chewer of khat on a daily basis, otherwise referred as occasional user:
- **Substance**: any of the drugs used by subjects, such as khat, tobacco, coffee, or alcohol;
- **Intensity**: frequency with which one uses khat-days, weeks, or months;
- Chronic chewer: use of khat for more than two years.
- Dental problems: comprised of dental caries (decay), and dental abscess as well as other complaints pertaining to teeth;
- **Dental caries** (**decay**): formation of cavities in the teeth by the action of bacteria accompanied by pain.
- **Dental abscess**: an infection of the mouth, face, jaw, or throat that begins as result of tooth infection or dental cavity;

- **Gastritis**: inflammation of the mucous membrane of the stomach;
- **Constipation**: straining on defectaion and passing of dry stool;
- Hemorrhoid: painful mass of swell in anal canal that leads to bleeding following defecation.

RESULTS

In the present study, a total of 1005 students aged between 18 - 30 years with mean age of 20.79 ± 1.39 participated giving a response rate of 98.6%. Seven hundred twenty (71.6 %) of them were males, 994(98.9%) were in the age group of 18-24 years and 412 (41.0%) of them were first year students (Table 1).

The prevalence of gastritis, constipation, hemorrhoids, and that of dental problems (carries, decay, filling and extraction) were 57.7%, 23.4%, 5.4% and 22.4%, respectively among all study participants (Table 1).

The current prevalence of khat chewing was 17.6%. More males, 155(87.6%, p < 0.001) than females, more students in the age group 18-24 years, 176(99.4%), than other age categories, more Muslims, 75(42.4%, p < 0.001) than other religion followers, more Oromos 114(64.4, p < 0.05%) than other ethnic groups were found to be khat chewers (Table 2).

As identified in binary logistic regression analysis, GI disorders were found to be higher among khat chewers than non chewers. As shown in table 2, 48.6% of the khat chewers had constipation with AOR 4.58, 95%CI [3.246, 6.46], p < 0.001; 71.8% of the chewers had symptoms of gastritis with AOR 2.173, 95% CI [1.52, 3.104], p < 0.001; 14.4% had hemorrhoids with AOR 4.92, 95% CI [2.82, 8.63], p < 0.001 and 36.2% had dental problems, AOR 2.35, 95% CI [1.65, 3.34], p<0.001.

Table 1: Association between sociodemographic characteristics and GIT disorders among Ambo University students, Ambo, Ethiopia, 2010, (n = 1005)

Socio-demographic variables		GIT Disorders Gastritis		Constipation		Hemorrhoids		Dental Problems	
		Yes (n =580) № (%)	No (n = 425) № (%)	Yes (n = 235) № (%)	No (n = 770) № (%)	Yes (n = 54) № (%)	No (n = 951) № (%)	Yes N (n = 225) (lo n =780) ½ (%)
Sex	Male Female X^2 , p-value	398 (68.9) 182 (31.4) 6.16, 0.008	322 (75.8) 103 (24.2)	173 (73.6) 62 (16.4) 0.59, 0.25	547 (71.0) 223 (29.0)	45 (83.3) 9 (16.7) 3.84, 0.03	675 (71.0) 276 (29.0)	166 (73.8) 59 (26.2) 0.65, 0.24	554 (71.0) 226 (29.0)
Age	18-24 25-30 X^2 , p-value	576 (99.3) 4 (0.7) 2.10, 0.13	418 (98.4) 7 (1.6)	233 (99.1) 2 (0.9) 0.19, 0.50	761 (98.8) 9 (1.2)	53 (98.1) 1 (1.9) 0.30, 0.45	941 (98.9) 10 (1.1)	221 (98.2) 4 (1.8) 1.3, 0.23	773 (99.1) 7 (0.9)
Religion	Orthodox Muslim Protestant Others* X^2 , p-value	319 (55.0) 132 (22.8) 102 (17.6) 27 (4.6) 8.4, 0.14	206 (48.5) 94 (22.1) 101 (23.8) 24 (5.6)	124 (52.8) 62 (26.4) 33 (14.0) 16 (6.8) 9.7, 0.1	401 (52.1) 164 (21.3) 170 (22.1) 35 (4.5)	24 (44.4) 16 (29.6) 9 (16.7) 5 (9.3) 0.01, 0.71	501 (52.7) 210 (22.1) 194 (20.4) 46 (4.8)	123 (45.7) 57 (25.3) 31 (13.8) 14 (6.2) 9.1, 0.11	402 (51.5) 169 (21.7) 172 (22.1) 37 (4.7)
Ethnicity	Oromo Amhara Tigre Others** X ² , p-value	375 (64.7) 133 (22.9) 26 (4.5) 46 (7.9) 5.33, 0.14	295 (69.4) 76 (17.9) 14 (3.3) 40 (9.4)	165 (70.2) 46 (19.6) 12 (5.1) 12 (5.1) 6.0, 0.11	505 (65.6) 163 (21.2) 28 (3.6) 74 (9.6)	45 (83.3) 6 (11.1) 1 (1.9) 2 (3.7) 7.12, 0.06	625 (65.7) 203 (21.4) 39 (4.1) 84 (8.8)	147 (65.3) 49 (21.8) 7 (3.1) 22 (9.8) 1.27, 0.73	523 (67.1) 160 20.5) 33 (4.2) 64 (8.2)
Year (Level) Cafeteria	First Second Third X^2 , p-value	248 (42.6) 186 (32.2) 146 (25.2) 5.7, 0.06	167 (39.3) 122 (28.7) 136 (32.0)	94 (40.0) 85 (36.2) 56 (23.8) 5.1, 0.08	321 (41.7) 223 (29.0) 226 (29.3)	23 (42.6) 17 (31.5) 14 (25.9) 0.13, 0.9	392 (41.2) 291 (30.6) 268 (28.2)	111 (49.3) 62 (27.6) 52 (23.1) 7.97, 0.02	304 (39.0) 246 (31.5) 230 (29.5)
Carciona	Users Non users X^2 , p-value	548 (94.5) 32 (5.5) 0.16, 0.40	404 (95.1) 21 (4.9)	222 (94.5) 13 (5.5) 0.84, 0.48	730 (94.8) 40 (5.2)	50 (92.6) 4 (7.4) 0.52, 0.32	902 (94.5) 49 (5.5)	215 (95.6) 10 (4.4) 0.42, 0.33	737 (94.5) 43 (5.5)

^{*} Wakefeta, Jehovah, Catholic, **Gurage, Somali, Harari, Welayta

Table 2: Binary logistic regression analysis to show association between khat chewing and GI disorders among Ambo University students, Ambo, Ethiopia, 2010 (n=1005)

Habit of khat chewing								
GI Disorders	Yes (n=177)		No (n=828)		AOR	95% CI	p-value	
		n	(%)	n	(%)			
Constipation	Yes	86	48.651.4	146	17.682.4			.000
-	No	91		682		4.581	3.246, 6.464	
Hemorrhoids	Yes	26	14.7	27	3.3	4.920	2.806, 8.625	.000
	No	151	85.3	801	96.7			
Gastritis	Yes	127	71.8	451	54.5	2.173	1 .521, 3.104	.000
	No	50	28.2	377	45.5			
Dental	Yes	64	36.263.8	159	19.280.8	2.346	1.651, 3.335	.000
problems	No	113	30.203.6	669	17.200.0	2.340	1.031, 3.333	.000

The magnitude of GI disorders increased with frequency of khat chewing where the disorders were highest among daily chewers. Constipation was found to be the problem of 80.0% of daily chewers. Hemorrhoid was found to be the problem of 25.0% of daily chewers and 5.6% of those who chew khat once per week. Gastritis symptoms were found to be the problem of

94.4% of students who chew khat once per week and 80.0% of daily chewers. Dental problems were found to be the complaints of 70.0% of daily chewers and 27.8% of those who chew khat once per week. Constipation and dental problems had statistically significant associations (p<0.05) with frequency of khat chewing as shown in Table 3.

Table 3: Association between frequency of khat chewing and GI disorders among Ambo University students, Ambo, Ethiopia, 2010.

GI Disorders	Frequen	cy of khat cl		p-value			
	On	Once/week			Daily		
	n	n % n		%			
Constipation	Yes	9	50.0	16	80.0		
	No	9	50.0	4	20.0	3.788	0.044
Hemorrhoids	Yes	1	5.6	5	25.0		
	No	17	94.4	15	75.0	2.684	0.115
Gastritis Symptoms	Yes No	17 1	94.4 5.6	16 4	80.0 20.0	1.730	0.205
Dental caries	Yes	5	27.8	14	70.0	(75)	0.011
	No	13	72.2	6	30.0	6.756	

Frequency of GI disorders also increased with duration of khat chewing where constipation, hemorrhoids, gastritis and dental problems were more prevalent among chronic chewers than those who chew khat for ≤ 2 years. Hemorrhoid and dental problems had statistically significant association (p<0.05) with duration of khat chewing habit (Table 4).

Table 4:- Association between duration of khat chews with GI disorders among Ambo University students, Ambo, Ethiopia, 2010.

	Durati	Duration of khat chewing					
GI disorders	< 2 Ye	< 2 Years		ars			
		n	%	n	%	\mathbf{x}^2	p- value
Constipation	Yes	31	36.0	55	64.0		
•	No	42	46.2	49	53.8	1.864	0.113
Hemorrhoids	Yes	6	23.1	20	76.9		
	No	67	44.4	84	55.6	4.150	0.032
Gastritis	Yes	47	37.0	80	63.0		
	No	26	52.0	24	48.0	18.447	0.202
Dental caries	Yes	20	31.3	44	68.8		
	No	53	46.9	60	53.1	4.13	0.030

DISCUSSION

This study found out that the current prevalence of khat chewing among Ambo University students was 17.6%. Each of the gastrointestinal disorders such as constipation, gastritis symptoms, hemorrhoids and dental problems were significantly higher among khat chewers than among non chewers.

Constipation could due be to sympathomimetic effect of cathinone, which is the active component of khat. Cathinone stimulates release of noradrenalin storage vesicles to produce CNS stimulation and peripheral sympathomimetic effects (9). Sympathetic stimulation inhibits colon motility and increases sphincter tone. As a consequence, excess water absorption by the intestinal epithelium results in the formation of hard stool leading to constipation (26). In a related study done in the whole mice, there was a significant reduction of gut motility when khat extract was given (27), and khat accounts for delayed intestinal absorption (11). Another study also reported that gastric emptying significantly delayed in volunteers who chewed khat leaves for 2 hours before the study (22, 30). This could be due to sympathetic stimulation since active the

ingredient of khat, cathinone, has sympathomimetic effect and sympathetic stimulation inhibits GI motility.

Hemorrhoid has shown a significant association with khat chewing (p < 0.001). Among the study participants, 26 (14.7%) of khat chewers had anal hemorrhoid. Among students who had hemorrhoid, 4(15.3%) of khat chewers students underwent hemorrhidectomy. Related reports from Yemen also confirmed the existence of significant association between chronic khat chewing and hemorrhoids (29).

The pathogenesis by which khat induces hemorrhoids could be: constipation, straining during defecation and prolonged sitting during khat chewing sessions, which may induce hemorrhoidal disease. In this study 15(57.7%) of the tudy participants with hemorrhoids have constipation. For the treatment of hemorrhoids, constipation should be treated first since it is probably the major cause of hemorrhoids (30).

There was a significant association between khat chewing and symptoms of gastritis (p < 0.001). In this study, 77.2% of khat chewers had at least one symptom of gastritis. This could be because of the presence of the strongly astringent tannis in khat (28) that may irritate the gastric mucosa leading to the inflammation and induce symptoms of gastritis. This finding is

supported by a related study conducted in Yemen to assess GI symptoms. According to the finding of the previous study, all gastritis symptoms were higher in khat chewers than non chewers (31).

There was a significant association between habit of khat chewing and dental problems (p<0.001). Previous studies indicated that khat chewers take much sugar, tea and/or coffee with sugar when they chew khat that can facilitate the growth and multiplication of bacteria, which could be association with dental problems (22, 30).

The prevalence of GI disorders increases with the frequency of khat chewing. Constipation and dental problems have significant association (p < 0.05) with frequency of khat chewing, suggesting that regular khat chewing could be a predisposing factor for constipation and tooth decay (28).

The prevalence of all GI disorders in this study was also higher among chronic chewers than those who chew khat for less than two years. Hemorrhoids and dental problems have shown significant association (p < 0.05) with duration of khat chewing. Constipation and gastritis are acute consequences of khat chewing and hemorrhoids and dental problems are its long term outcomes (30).

Based on the the findings, it was concluded that khat chewing is a common practice among university students. The result of this study depicts that GI disorders are significantly associated with khat chewing. According to this study, the prevalence of GI disorders increases with frequency of khat chewing as well as duration of the habit. Using the present study as a base line data, further large scale study on the adverse effect of khat chewing on GIT is highly recommended. Community-based health education to is also needed.

ACKNOWLEDGMENTS

The authors are grateful to Jimma University Research Office for its financial support.

We would like to thank Ayalkibet Jiru, Desta Thushune, Hailemarian Hailesilasiie, and Kenfe Tesfaye for general support in Jimma, and Bianka Leitner, Fabian Jacobs, Florian Boss, Florian Seemüller, Josef Christan, Karin Koelbert, Laurenz Wurzinger, Michael Meyer, Nico Kühner, Paula Messner, Richi Musil, and Thomas Ludwig for general support in Munich. Special thanks go to the first-year medical students in Jimma and Munich! We thank also Jacquie Klesing, ELS, for editing assistance with the manuscript.

REFERENCES

- 1. Cox G and Rampes H. Adverse effects of khat: A review. *Advances in Psychiatric Treatment*. 2003; 456-463.
- 2. Nencini P, Grassi MC, Botan AA, Asseyr AF and Paoli E. Khat chewing spread to the Somali community in Rome. *Drug Alcohol Depend*. 1988; 23: 255-158.
- 3. Al Motarreb A, Baker K. and Broadley KJ. Khat: Pharmacological and Medical Aspects and its social use in Yemen. *Phytother. Res.* 2002; 16: 403-413.
- 4. Nordal A. Khat: Pharmacognostical Aspects. *Bull Narc.* 1980: 32:51-64.
- 5. WHO Report. Review of the Pharmacology of Khat. *Bull Narc*. 1980; 32:83-93.
- 6. Elmi AS. Khat Consumption and problems in Somalia. Proceedings of the International Conference on Khat. Antanarivo, Madagascar. 1983: 17-21.
- 7. Kalix P. The pharmacology of khat. *Gen Pharmacol*. 1984; 15: 179-187.
- 8. Ishraq DB and Jiri SB. Khat Habit and its Health Effect. A Natural Amphetamine. *Biomed Papers*. 2004; 148(1): 11–15.
- 9. Hughes P. Khat chewing in Yemen: International council on alcoholism and addictions. Abstracts of the Fourth International Institute on the Prevention and Treatment of Drug Dependence. Lausanne, Switzerland. 1973; 32–46.
- 10. Molham Al-Habori. The Potential Adverse Effects of Habitual use of *Catha edulis* (khat). *Expert Opinion on Drug Safety*. 2005; 4 (6): 1145-1154.

- 11. Kalix P. Khat: A plant with amphetamine effects. *J Subst. Abuse Treat.* 1985; 163-169
- 12. Martin D, Schechter J, Rosecrans A, and Richard AG. Comparison of Behavioral Effects of Cathinone, Amphetamine and Apomorphine. *Pharmacol Biochem Behav*. 1984; 20 (2): 181-184.
- 13. Kalix P and Braenden O. Pharmaco-logical aspects of the chewing of khat leaves. *Pharmacological Reviews*. 1985; 37: 149-164.
- 14. Kalix P. The Pharmacology of Khat. International Symposium, Addis Ababa. 1984; 69-73.
- 15. Amaha M. Clinical Aspects of Khat (*Catha edulis* Forsk): In Proceedings of the International Symposium on Khat. 1983; 77-83.
- Atalay A, Dereje K. and Kullgren G. The prevalence and socio-demographic correlates of khat chewing in Butajira, Ethiopia. Acta Psychiatry, 1999; 397: 84-91.
- 17. Andualem M and Zeleke M. Khat (Catha edulis Forsk) chewing, socio-demographic description and its effect on academic performance, Jimma University students. *Ethiop Med J.* 2004; 42(2):125-136.
- 18. Kalayu M, Andualem M. and Yeshigeta G. Effect of substance use on academic achievement of health officer and medical students of Jimma University, Southwest Ethiopia. *Ethiop J. Health Sci.* 2009; 19(3): 155-163.
- 19. Selassie SG and Gebre A. Rapid assessment of drug abuse in Ethiopia. *Bull Narc*. 1996; 48: 53-63.
- 20. Marsh PD: Are dental diseases examples of ecological catastrophes? *Microbiology*. 2003; 149 (2): 279-294.
- 21. Selwitz RH, Ismail AI. and Pitts NB. Dental caries. *Lancet*. 2007; 369(9555): 51-59.
- 22. Heymann TD, Bhupulan A, Zureikat NE, Bomanji J, Drinkwater C, Giles P. and Murray-Lyon IM. Khat chewing delays gastric emptying of a semi-solid meal. *Aliment. Pharmacol. Ther.* 1995; 9(1): 81-83.

- 23. Yigzaw K. Cigarette Smoking and Khat Chewing among College Students in North West Ethiopia. *Ethiop. J Health Dev.* 2002; 16(1): 9-17.
- 24. Gunaid AA, EL-Khally FM, Hassan NA. and Murray-Lyon IM. Chewing Qat leaves slows the whole gut transit time. *Saudi Med J.* 1999; 20: 444-447.
- 25. Smart RG, Huges PH and Jonsten LD. Methodology for student drug abuse survey. World Health Organization Offset Publication. 1980; Number 55.
- 26. Stefan ML and Dtsch AI. The pathophysiology, diagnosis, and treatment of constipation. *Eth. Pharmaceutical J.* 2006; 24(2): 116-124.
- 27. Eyasu M. Constipating and Spasmolytic Effects of Khat (Catha edulis Forsk) in Experimental Animals. *Phytomedicine*. 2000; 7(4): 309-312.
- 28. Daisy A, Carlos A, and Hildegardo C. Evaluation of constipation. *Am Fam Physician*. 2002; 65: 2283-2290.
- 29. Al-Hadrani AM. Khat induced hemorrhoidal disease in Yemen. *Saudi Med J.* 2000; 21: 475-477.
- 30. Luqman W. and Danowski TS. The use of khat (Catha edulis) in Yemen. Social and medical observations. *Ann Intern Med.* 1976; 85: 246-249.
- 31. Sikirov BA. Management of hemorrhoids: a new approach. *Isr. J. Med. Sci.* 1987; 23 (4): 284–286.
- 32. WHO Advisory Group, Review of the pharmacology of khat. Bulletin on Narcotics. 1980; 32: 83–93.
- 33. Heymann TD, Bhupulan A, Zureikat NE, Drinkwater C, Giles P, Murray-Lyon IM. Khat chewing delays gastric emptying of a semi-solid meal. Alimentary Pharmacology and Therapeutics. 1995; 9: 81–83.
- 34. Gunaid AA, El-Khally FM, Hassan NA, Murray-Lyon IM. Chewing qat leaves slows the whole gut transit time. Saudi Medical J. 1999; 20: 444–447.
- 35. Eyassu M. Constipating and spasmolytic effects of khat (Catha edulis Forsk) in experimental animals. Phytomedicine 2000; 74: 309–312.