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DEPARTMENT OF PHYSIOLOGY

The effect of Catha Edulis (khat) on blood pressure, pulse rate, and blood glucose concentration, in adult subjects of Arba Minch town, southern Ethiopia.

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A Thesis Submitted to the School of Graduate Studies, Addis Ababa University College of Health Science, School of Medicine, and Department of Physiology in Partial Fulfilment of the Requirement of Master's Degree in Medical Physiology

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MSc THESIS

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LIST OF ABREVIATION AND ACCRONYM

AAU…….....Addis Ababa University

ABP……..……Arterial Blood Pressure

AC……...Adenyl Cyclase

APA ……Amphetamine

AR……...Adreno-receptor

BP……Blood Pressure

BPM……Beats per minute

CAMP…….Cyclic Adenosine Monophosphate

C. edulis …….Catha edulis

CHS……College of Health Sciences

CNS…….Central Nervous System

CSA…….Central Statistical Agency

CVS…….Cardio Vascular System

CTN……Cathinone

DBP…….Diastolic Blood pressure

FBS……..Fasting Blood Sugar

Gc-coupeled……G-protein coupled receptor

HIV……..Human Immune Viruses

HR……Heart Rate

ISA……...…Indirect Acting Sympathomimetic Amines

MAP…….Mean Arterial Pressure

MFBS……...Mean Fasting Blood Sugar

NA……Nor Adrenaline

NIDA……National Institute of Drug Abuse

NIDIC……...National Drug Intelligence Center

SBP……Systolic Blood Pressure

SOP……...Standard Operating Procedure

TAAR…….....Trace Amine Associated Receptors

WHO……World Health Organization

ABSTRACT

Background: In Ethiopia khat chewing had deep rooted history as early as fourteenth century and is commonly used for social, religious and recreational purposes. Recently, khat chewing became a common practice among secondary, high school, higher education institution's students and younger generation. It has been established that the leaves of khat comprise an active psycho stimulant substance known as "cathinone" that is analogous in structure and pharmacologic action to amphetamine. Though, numerous case reports of khat induced psychoactive and metabolic profiles have been published; investigations in Arba Minch city (Southern Ethiopia) remain limited.

Objectives: To assess the acute effect of khat chewing on blood pressure, pulse rate and blood glucose concentration in adult subjects adapted to chewing khat in Arba Minch town.

Methods: Comparative cross section study design using simple random sampling technique was employed to select khat chewers and controls. 128 khat chewers (age: above ≥18 years), non-chewers – controls (age: ≥18 years) from both sexes participated in the study. Structured questionnaire were used to document the socio demographic characteristics and clinical status of the study partakers. Pulse rate (PR/min), blood pressure (mm Hg) and fasting blood glucose level (mg/dl) were measured and recorded. Data were analyzed via EPINFO (ver. 7) SPSS (ver. 23) respectively.

Results: Khat chewers have showed significantly higher values than non-chewers controls for blood glucose (97.2±21.7 *vs* 88.2±16.8, *P=0.000*), systolic (118.0±16.6 *vs* 112.0±12.148, *P*=0.003), diastolic (78.8±14.7 *vs* 72.9±11.2, *P=0.001*), mean arterial blood pressure (90.4±18.4 vs 84.6±15.2, P=0.001) and the mean pulse rate (77.6±34.6 *vs* 72.8±31.887, *P*=0.000).From 17.1% of the study participants screened for hypertension among the chat chewers was 8.6%. A total of 18.6% study partakers were screened for tachycardia of which 13.2% were khat chewers and 5.4% were non-chewers. And a total of 20.2% study participants were screened for hyperglycemia of which, 14.0% were khat chewers and 6.2% remained non-chewers.

Conclusion: Khat chewing in Arbaminch town has induced marked changes in blood pressure, heart rate, and hyperglycemia, factors which are known to be positively associated with cardiovascular and metabolic diseases.

Key words*:* *Blood pressure, pulse rate and blood glucose concentration*

1. Introduction

1.1. Background of the study

Catha edulis, commonly known as Khat, Qat, Chat or Miraa (Becklerleg, 2010) is a flowering shrub which is small to medium sized ever green tree that is categorized to the Celastraceae family. It is cultivated as a bush or small tree mostly in Yemen and East Africa countries (Elhassan *et al.,* 2014; Zewdineh, 2014). The shrub raises to a height of 6 meters and the leaves are leathery, glossy, brownish green, with serrated edges, arranged in an alternate manner on straight branches. The chewing of young and fresh leaves of Catha edulis Forsk. Variously referred to as Khat, Chat, Abyssinian tea, and are used for their psychoactive properties (Cox, 2003; Zewdineh, 2014).

Chewing the shrubberies of the plant entitled khat (Catha edulis Forsk) is communal custom in several nations of East Africa and the Arabian Peninsula. Currently its usage has spread out to Northern America and Europe, predominantly among emigrants and refugees from countries like Somalia, Ethiopia, Yemen (Balint *et al*, 2009); khat is intense stimulant that is a reason for a mild to moderate psychological dependency, Although not strong stimulant as that of tobacco and alcohol, and it can have considerable health and economic consequence (CSA, 2010). Consistent khat consumption found to associate with increased diastolic blood pressure among adults in Ethiopia (Getahun *et al.,* 2010).

In the year 1237 the effect of Catha edulis were declared for the first time in the literature called “The Book of compound drug” written by Arabian physician Naguib Ad Din. The author suggested that khat would be used in the treatment of depression, and also as mood enhancer at social assembly. Other historic sources state that khat was given to Territorial Army to counter fatigue and chewing khat for invigilators and recreations is alleged to have originated in the regions around the southern part of the red sea. For more than 800 years ago (Asha and Renee, 2010). In Ethiopia khat chewing had deep tooted history as early fourteenth century and is commonly used for social and religious purpose. Additionally, it was considered as recreational substance. Recently, chat chewing becomes common practice among secondary, high school and higher education institution students and younger generation. (Wakgari and Aklilu, 2010).

General factors including normalization in the community (Odenwald *et al.,* 2010), social mobility accessibility (affordability and convenience) of khat leaf in the whole year and importance of khat leaf as cash crop has been recognized as a major contributors to the widespread of khat chewing habit (Megerssa *et al.,* 2014).

1.2. Statement of the problem

With the improved highway and air transport conveyance in this period, khat possibly be distributed toward different sites of the world. Connotation among khat chewing a lot of somatic mental health complications have been recognized (Odenwald et al., 2013) indicating it as essential to apprehend public health issues and clinical medicine. To indicate certain, raised arterial blood pressure (Getahun et al., 2010; Tesfaye et al., 2008), acute myocardial oxygen demand and supply imbalance, hemorrhoid, constipation, duodenal ulcer and inhibition of sperm cell production have been stated to be concomitant with khat chewing (Almotarreb *et al.,* 2010; Cox *et al.,* 2003). In enormous viewpoints multicenter study of patients with acute coronary syndrome, khat chewing was linked with greater jeopardy of in hospital mortality and cerebrovascular stroke (Ali *et al.,* 2010). In recent time, measurement criteria's of substance dependency syndrome were revealed in different studies among khat chewers and using it for a long period time persuade to physical enslavement (Kassim *et al.,* 2013).

Khata is a plant or tree whose leaves foliage's have been masticated and swallowed for a variety of reasons for a centuries around East Africa and Arabian peninsula and exported to consumers who are situated in different parts of the continent near and far via different transport mechanisms (Toennes *et al.,* 2003). Approximately 10 million folks chew khat (Catha edulis) globally. An enormous studies in Yemen indicates that, eighty two percent of men and forty three females testified that they have a minimum of one in their life time incident of khat chewing and forty percent of users progressively developed tolerance to and dependence on the plant (NIDA, 2011).

World health organization categorized khat as a drug of abuse. The energizing substance khat is recognized as abusive substance in Norway due to its effects like amplified alertness, elation, excitement and sometimes psychosis and increased activity in peripheral sympathetic nervous system followed by palpitation, raised arterial blood pressure and red eyes (Al-samarraie, 2007;

Forden, 2007). Varying from minor to complex psychological dependency is observed by users (Bruce, 2010). Using khat for extended period of time could be a reason for different health problems like insomnia, depression, loss of appetite and gastric problems and cardiovascular system pathologic conditions like myocardial infarction (Balint *et al.,* 2009 and Corkery *et al.,* 2011).

A large population survey in Southern Ethiopia, Butajira town showed that, from the total sample size of 10,468 adult's, from the study partakers 55.7% of had used Catha edulis at same point in their life, 50% were using it until now and 17.4% described using on regular basis. Additionally the result showed khat consumption was concomitant with being male, Islam religion follower (80% of current chewers used the plant to gain its advantage of increased concentration for prayer), to achieve a better score in educational institutions and smoking cigarette. Following khat chewing taking alcohol or sometimes drugs like marijuana predispose users to HIV and other sexually transmitted infection in Ethiopia, by motivating people to engage in unsafe sex and sometimes unintended pregnancies could occur (Kebede et al., 2015 and Dawit et al., 2006). For juvenile, allowing to practice khat chewing could bring several risks. Many circumstances negatively influence and upsurge the susceptibility of adolescent to HIV AIDS and other threats to their health and wellbeing, the consequence could be Biological or social (Jeftha, 2006).

1.3. Significance of the study

Catha edulis plant is extensively used in different parts of Ethiopia; particularly high school, and tertiary educational institution's learners. Even though, there are abundant studies on the effect of khat on the behavior and cognitive variations of khat in human being, additionally they are not all-inclusive and numerous available studies have been carried out in the perspectives of observational and single case studies. Khat consumers are possibly in a greatest rate of non-appearance from the class room and meagre academic enactment (Mulugeta, 2013). Despite the fact, comparable few studies have been carried out regarding its effect in the cardiovascular system metabolic alteration. As a result, this thesis will be conducted to assess the acute effect of Catha edulis on blood pressure, pulse rate and blood glucose concentration among Arbaminch town chat chewers. Following the finding of the study, diverse schemes will be made to build cognizance of health and health related impact of khat chewing for the users like motor vehicle and taxi drivers, high school and higher institution students specifically and general public through the responsible authorized body.

2. LITERATURE REVIEW

2.1. Botanical description of Catha Edulis (khat)

Khat belongs to the kingdom Plantae, class Magnoliopsida, order Celastrases, family Celastraceae, genus Catha and species edulis. The shrub khat (Catha edulis Forsk) has a slender trunk with smooth, thin bark. The lancet shaped leaves are between 0.5cm and 5cm wide. Young leaves are reddish-green, later turning to yellow-green (Figure 1). The leaves are faintly aromatic, with a stringent, slightly sweet taste. The tap root grows to a depth of 3m or more. In the area with frost, the shrub can grow higher than 1.5m but in places with more rainfall, such as the highland of Ethiopia and areas near the equator, khat trees can reach up to 20m. Khat can also survive drought, when other crops fail. It grows at altitude of 1500m-2000m. Khat is a perennial propagated by grafting. Trees grow for 3-4 years before leaves are harvested. A healthy trees yield for about 50 years. Khat is not affected by any known disease (Al-Motarreb *et al.*, 2002; NDIC, 2008).

Khat is the only species in Celastraceae that is cultivated on a large scale specifically for its stimulant alkaloids. Cultivated khat is primarily propagated clonally via rooted cutting and trained in to several forms from low growing shrubs resembling cultivated tea plant, to narrow upright trees, and open downward trained trees (Carrier, 2007). The color of young stems and leaves is the primary trait by which farmers and traders distinguish different cultivars. Additionally the flavor, potency, and agronomic attributes, such as tolerance to different growing conditions and growth habit, are often used to differentiate khat cultivars (Lemissa, 2001; Carrier, 2007). It is difficult to speculate as to what environmental factors might be causing a stem color change between individuals in such close spatial proximity. However, light intensity and temperature have been shown to be important in influencing the expression of anthocyanin's and might be relevant for khat coloration (Lightbourn *et al.*, 2007).

Figure 1: *A picture which shows young khat shrub*

2.2. Phytochemical studies of Catha Edulis (Khat)

Many different compounds are found in khat, including alkaloids, terponoids, flavonoids, sterols, glycosides, tannins, amino acids, vitamins and minerals (Cox *et al.,* 2003). The Phenylalkylamines and cathedulins are the major alkaloids. The cathedulins are based on a polyhydroxylated sesquiterpene skeleton and are basically polyesters of euonyminol; 62 different cathedulins have recently been characterized from fresh khat leaves (Kite GC *et al.,* 2003). The khat Phenylalkylamines comprise cathinone (s-[-] cathinone), which is the primary constituent of khat, as well as two diastereoisomers: cathine (1S, 2S - [+]- nor pseudoephedrine or [+] norsendoephedrine) and norephedrine (1R, 2S -[-]-norephedrine), which are the secondary constituents. These compounds are structurally related to amphetamine and noradrenaline. Cathinone is found mainly in the young leaves and shoots (Kite GC *et al.,* 2003). The plant contains the (-) - enantiomer of cathinone only; the (+) - enantiomer is not found. Thus the Naturally occurring S-(-) cathinone has the same absolute configuration as S-(+) as S-(+) - amphetamine. Hence the name of Catha Edulis: “A plant, with naturally occurring

amphetamine"but now a days in the USA some times it is mentioned as “herbal ecstasy” (Carrier, 2007) (Kuczkowski, 2005).Khat leaves also contain considerable amount tannins and flavonoids (Almotarreb *et al.,* 2002; Hassan *et al.,* 2002). Chemical Formulae: Cathinone: $C_9H_{11}NO$, Cathine and nor-ephedrine: $C_9H_{13}NO$. Chemical Names: Cathinone: S-(–)-cathinone; S-(–)-α-aminopropiophenone; (S)-2- amino-1-Phenyl-1- propanone; Cathine: 1S, 2S-(+)-nor pseudoephedrine; 1S, 2S-(+) - phenylpropanolamine; 2-amino-1-phenyl-1-propanol; Nor ephedrine: 1R,2S-(–)-nor ephedrine; 1R,2S-(–)- phenylpropanolamine; 2-amino-1-phenyl-1-propanol. Relative molecular mass (Mr): Cathinone: 149.2 Cathine and norephedrine: 151.2

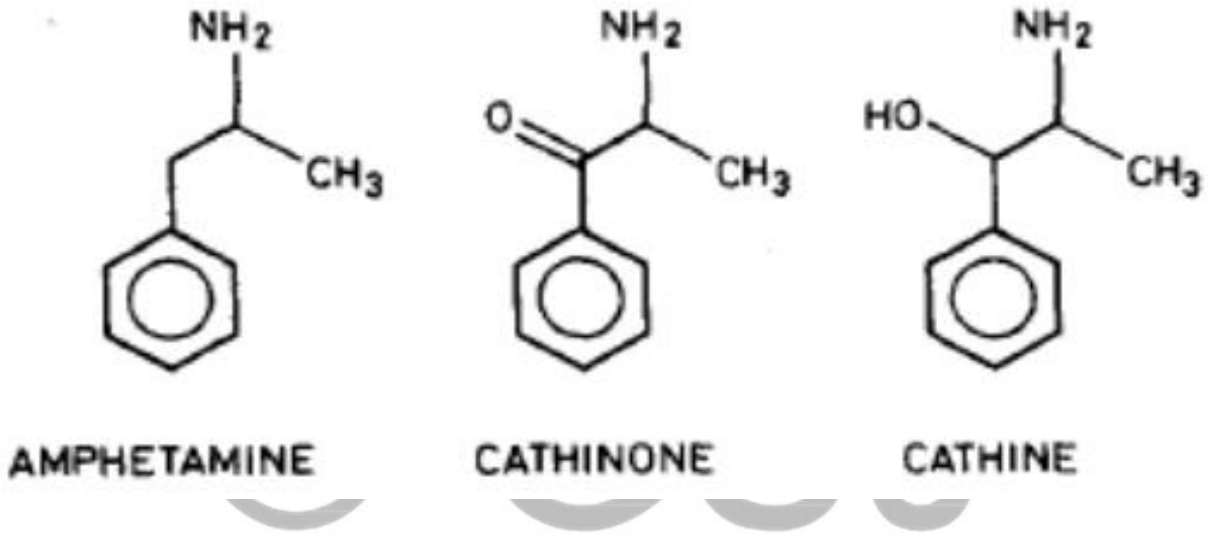

Figure 2: *The chemical structure of khat alkaloids in comparison with amphetamine*

The main psychoactive component of khat explains why fresh leaves are preferred and why khat is wrapped in banana leaves to preserve freshness. Khat taste varies depending on tannic-acid content; Khat leaves have an astringent tastes and aromatic odour, with the young leaves being slightly sweet (WHO, 2006). Chewing the material effectively liberates the alkaloids from the leaves and allows rapid absorption in to the systemic circulation (Toennes SW, 2003).

2.3. Modes of Action

Khat contains a number of pharmacologically active compounds in leaves and young shoot such as the phenylpentenylamines, cathedulins and the most important major and natural alkaloids of d-(+)- amphetamine like action and structure; Cathinone (Granziani *et al.,* 2008). Cathinone is relatively unstable and rapidly metabolized to nor pseudoephedrine (Cathine) and nor ephedrine (Al-Motarreb *et al.,* 2002).

Cathinone is released within 15-45min during chewing and peak plasma level of cathinone is obtained 1.5-3.5h after the onset of chewing khat (Granziani *et al.,* 2008). Apparently, (–) cathinone shares important effects of (+)-amphetamine on neurotransmission. Further evidence for serotonergic involvement is given in a recent study in which both khat extract and cathinone produced a significant depletion of serotonin and its metabolite 5-hydroxyindoleacetic acid in both the anterior and posterior striatum (Banjaw *et al.,* 2005). Cathinone has vasoconstrictor activity in isolated perfused hearts from guinea pigs (Al-Motarreb *et al.,* 2003). The effect was unlikely to be due to an indirect action by release of noradrenaline from sympathetic nerve endings or due to a direct action on alpha1-adrenoreceptors. (–)-Cathinone is able to potentiate noradrenaline-evoked contractions of the rat right ventricle (Cleary *et al.,* 2002) and to inhibit the uptake of noradrenaline into ventricular slices by a mechanism involving competitive blockade of the noradrenaline transporter. The vasoconstrictor activity of cathinone explains the increase in blood pressure seen in humans (Cleary *et al.,* 2002). The sympathomimetic actions of cathinone would be expected to raise plasma catecholamine levels. These catecholamines would increase blood glucose levels by activation of glycogenolysis in skeletal muscles and the liver; a β2-adrenoceptor-mediated response. There is also inhibition of insulin release from the pancreatic β -cells via α2-adrenoceptor stimulation which would also elevate blood glucose levels (Saif-Ali *et al.,* 2003). When taking khat, large amount non-alcohol drinks are consumed. There is pharmacological synergism with drinks containing methyl xanthines (e.g. tea and cola), which therefore enhance the effect of khat (Cox and Rampes, 2003).

2.4. Effect of Khat Chewing on Cardiovascular System

Structural mimicry between khat constituents and indirectly-acting sympathomimetic agents allows it to activate the sympathetic nervous system, thereby elevating the blood pressure and the heart rate (Ali WM *et al.,* 2011). Specifically, the impact of khat and ethanolic extracts of its active constituent, cathinone, on the cardiovascular system (CVS) parameters of heart rate (HR) and blood pressure (BP) have been reported from different settings (Al-Hashim *et al.,* 2012; Ali WM *et al.,* 2012; Al-Motarreb AL *et al.,* 2002). Studies that attempted to explore the mechanism of action of khat effect on heart rate are scant. A human, double-blinded, 3 arm cross-over, placebo-controlled study (n=63; all male)involving khat, indoramin (selective α1-blocker) and atenolol (selective β1-blocker), showed that atenolol could potentially reduce ($p<0.05$) the significantly elevated heart rate induced by khat, but could not do so for elevated heart rates as a

result of indoramin administration (Hassan NA *et al.,* 2005). This suggests that heart rate acceleration among khat chewers is mediated by β1-adrenoceptors rather than α1-adrenoceptors. Once activated, a G-protein coupled receptor (Gs-coupled ß1-adrenoceptor) dissociates, activates adenylyl cyclase (AC), and increases cytosolic cyclic adenosine monophosphate (cAMP) which activates Ca2+ channels (Backer DE *et al.,* 2012). This Ca2+ influx promotes actin myosin interactions, increases heart contraction forces, and causes tachycardia (Backer DE *et al.,* 2012). Definitive knowledge of a direct effect of khat or cathinone at the receptor level is lacking. Nevertheless, the structural similarity between cathinone and amphetamine allows for cathinone functioning as an indirectly-acting sympathomimetic agent. Amphetamine could promote the release of monoamines and reduces their reuptake, thus, increasing dopamine, noradrenaline and serotonin levels in the synaptic cleft (El-Menyar *et al.,* 2015). This causes sympathetic over-activity and tachycardia. So, if cathinone could act like amphetamine in causing sympathetic over-activity, this would highlight a central, rather than peripheral effect of khat or cathinone on heart rate (El-Menyar *et al.,* 2015). Khat typically is ingested which chewing the leaves. After ingested khat, the chewers experience an immediate increase in blood pressure and heart rate. Various reasons have been given for chewing khat. Most chewers used khat to gain good level of concentration for prayers. Some chewers reported that khat intake results in increased energy level and alertness enhance imaginative ability and the capacity to associate ideas and improve the ability to communicate (Basker, 2013).

A comparative study conducted in Butajira to assess regular khat (Katha Edulis) chewing on blood pressure showed that the prevalence of hypertension was significantly higher among khat chewers than non-chewers. A considerably high proportion of chewers than non-chewers had sub-optimal diastolic blood pressure (>80mmhg). The mean (SD) diastolic blood pressure was significantly higher among khat chewers than non-chewers. Similarly, khat chewers had significantly higher mean (SD) heart rate than non- chewer's .There was no significant different in mean systolic blood pressure between the two groups (Getahun *et al.,* 2010). Regular khat chewing is associated with elevated mean diastolic blood pressure (Tesfaye *et al.,* 2008). In guinea-pig isolated perfused hearts, cathinone causes a marked constriction of the coronary vasculature, the maximum being equivalent to that achieved with noradrenaline or the cathinone metabolite, nor pseudoephedrine. There was also a pronounced negative inotropy, possibly due to the impaired coronary perfusion (Al-Motarreb and Broadley, 2003). The vasoconstriction was

not inhibited by cocaine (10 µM) suggesting that the response was not an indirect sympathomimetic action. Cathinone and MDMA both produced coronary vasoconstriction in pig isolated left anterior descending coronary artery rings. The vasoconstrictor response to cathinone was also not inhibited by cocaine or the1-adrenoceptor antagonist, prazosin (Fig. 3) (Baker *et al.*, 2007). The increase in blood pressure after chewing khat was also not blocked by the 1-adrenoceptor antagonist, indoramin, confirming a lack of involvement of vascular 1-adrenoceptors in the pressor response (Hassan *et al.*, 2005).There is probably a significant cardiac component to the increase in blood pressure after chewing khat through tachycardia, since the increases in blood pressure and heart rate were reduced by the α1-adrenoceptor antagonist, atenolol (Hassan *et al.*, 2005). Cathinone can act as an indirectly acting sympathomimetic amine (ISA mechanism) through uptake in to sympathetic neurons and release of noradrenaline (NA) on to-adrenoreceptors. It can also act via a sympathomimetic-independent mechanism probably directly on trace amine-associated receptors (TAAR mechanism) figure 3 below.

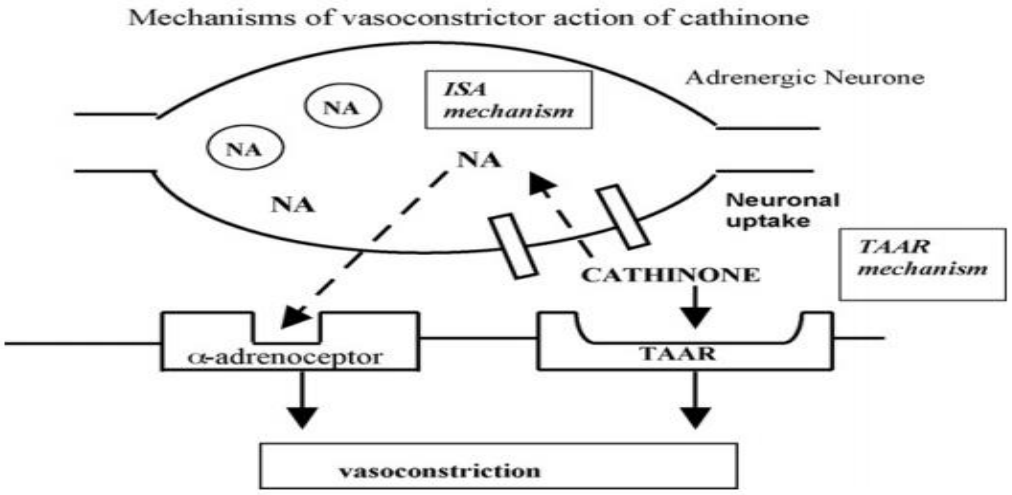

Figure.3: *Mechanisms of the vasoconstrictor actions of cathinone.*

2.5. Effect of Khat Chewing on Blood Glucose

Rabbits fed a diet containing different levels of khat leaves showed an increase in plasma glucose levels after 4 months but a significant reduction after 6 months (Al-Habori and Al-Mammary, 2004). These results are difficult to interpret but indicate the complex relationships between the stimulation of glycogenolysis by raised catecholamine levels and the effects of raising glucose on insulin release. Raised glucose levels will result in compensatory increases in

insulin release. This study also showed that feeding rabbits with khat caused a significant reduction in plasma cholesterol throughout the 6-month period (Al-Habori and Al-Mammary, 2004). This of course would be a favorable consequence of khat chewing in the context of cardiovascular risk. Clearly, our knowledge about the effects of cathinone and khat chewing on plasma glucose and insulin levels is very sparse and controlled studies need to be undertaken. These should examine the effects of acute cathinone administration and khat chewing on fasting levels of glucose, insulin and adrenaline in the serum. The effects of α2-and β-adrenoceptor antagonists on these changes could then be examined to dissect out the possible mechanisms and interactions between these factors. Effects of khat chewing on appetite may also indirectly influence blood glucose levels and body weight. Recently, Murray et al. (2008) showed chewing khat to significantly decrease subjective feelings of hunger and increase the sensation of fullness but had no effect on ghrelin and peptide YY levels.

They concluded that the anorexigenic effect of khat may be secondary to central mechanisms mediated via cathinone. Indeed, one of its uses is in the control of obesity, which indirectly would reduce the risk of diabetes. High plasma levels of the anorectic hormone, leptin, have been found 4 h after a heavy khat chewing session (400 g). This hormone may then contribute to the decreased appetite and body weight observed in khat chewers (Al-Dubai *et al.*, 2006). Cathinone releases catecholamines (noradrenaline/adrenaline) which activate 2-adrenoceptors (2-AR) in the liver to induce glycogenolysis of glycogen to glucose. They also activate pancreatic 2-adrenoceptors (2-AR) to inhibit insulin release, which normally increases glucose uptake by skeletal muscle; the inhibition of insulin therefore results in increased blood sugar. High blood sugar induces insulin release to enhance uptake of the elevated glucose levels.

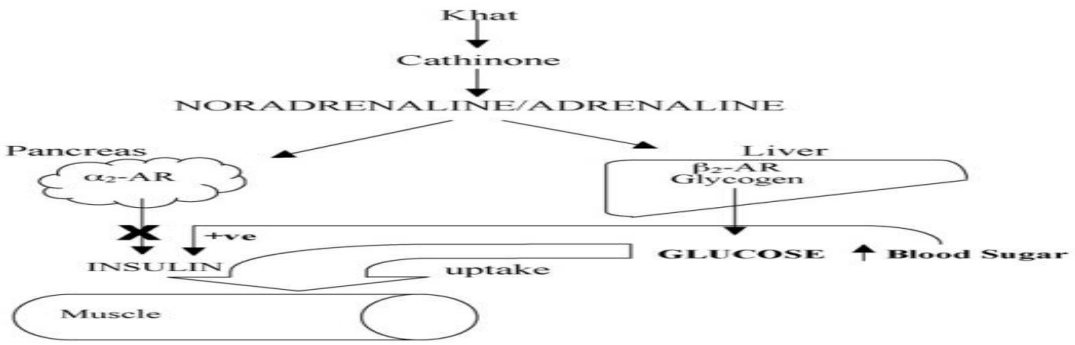

FIGURE.4: *diagram of the hypothetical effects of khat and cathinone on blood sugar levels.*

2.6. Conceptual framework of the study

Chat is chewed mainly for stimulating effect. The major component of khat is Cathinone, has a high potential for abuse, no currently accepted medical use in treatment. In addition to its central effect it has diverse adverse systemic effect on the body. Moreover, the effect of khat is becoming worldwide concern particularly in the khat producing countries, mainly, because of the argument in the scientific community and the economic, social, psychological and physical influence on human. There is a confusion weather chat should be legal or not. The study focused on the acute effect of chat ingestion on blood pressure, pulse rate and blood glucose concentration. In addition chat ingestion can have an effect on the body system which are not included in the study and not studied well. Its effect on cardiovascular system and glucose metabolism is mentioned a few. The cardiovascular system is a major system with a vital function to our normal body activities and to meet the metabolic demand of our body systems.

Tests which measure how well the cardiovascular system performing and metabolic activities takes place is important to know the health status of individuals, these mentioned vital activities can be measured by different techniques, like blood pressure, pulse rate and blood glucose concentration have been used in this study.

3. OBJECTIVE OF THE STUDY

3.1. General objective:

- To assess the effect of acute khat chewing and its effect on blood pressure, pulse rate and blood glucose concentration in adult subjects adapted to chewing khat in Arba Minch town, southern Ethiopia.

3.2. Specific objectives:

- To assess the acute effect of khat chewing on blood pressure.
- To assess the acute effect of khat chewing on pulse rate.
- To assess the acute effect of khat chewing on fasting blood glucose level.

4. HYPOTHESIS

4.1. Null Hypothesis (Ho)

- There is no association between acute khat chewing and systolic and diastolic blood pressure
- There is no association between acute khat chewing and pulse rate
- There is no association between acute khat chewing and blood glucose concentration

4.2. Alternative Hypothesis (Ha)

- There is association between acute khat chewing and systolic and diastolic blood pressure
- There is association between acute khat chewing and pulse rate
- There is association between acute khat chewing and blood glucose concentration

5. MATERIALS AND METHODS

5.1. Description of Study Area

The study was conducted in Gammo Zone (Arbaminch town) Southern Nation Nationalities and People Regional State (SNNPR).The Town is located between 6°01'59"N latitude and 37°32'59" longitude. Arba Minch town is located Southern Ethiopia at a distance of 505 km from the capital city Addis Ababa.

5.2. Study Period

Study was conducted from December 2019 to February 2020.

5.3. Population

5.3.1. Source Population

All khat chewers from Arba Minch community.

5.3.2. Study Population

Study subjects: All adults aged 18 years old and above residing in Arba Minch town for more than six months prior to the study and those who met the inclusion criteria for the study.

Control subjects: Non-chewers with similar age group to the study subject who fulfill the inclusion criteria for the control group.

5.4. Study design and sampling Technique

Comparative cross sectional study using simple random sampling technique were employed to select study participants from the source population and proportionate allocation method was used to determine sample size of each group. Participants Subjects who had history of khat chewing were selected as study (exposed) groups and non-chewers with the same age group to the exposed subjects were taken as a control groups.

5.5. Determination of sample size

To determine the sample size of the proposed, study, the likely percentages for exposed group is (47 %) and the likely percentage value for control was (45%) (Workineh *et al,* 2010). Sample size is calculated using the double population proportion formula: n (in each group) = *(P1q1 + P2q2) ((z1-α/2+ z1-β) 2 (P1 –P2)2,* Where: P1 = the likely percentage of exposed group = 47% = 0.47; q1 = 1-P1= 0.53; P2 = the likely percentage of control group = 45% = 0.45; q2 = 1-P2= 0.55 α = the significance level = 0.05, β = 0.1 1 –β = the power of test 90% z (1-α/2) = 1.96 =value of the standard normal distribution corresponding to 0.05 significance level.

Z (1-β) = 1.28 = value of the standard normal distribution corresponding to the 90% level of power n (in each group) = ((0.47 × 0.53) + (0.45 × 0.55)) (1.96 + 1.28)2 (0.47 – 0.45)2 = **128.** Based on the calculation, the determined sample size in each group was 128 and assuming non-response rate of 10% of the calculated sample size were, 128 × 10% = 12.6 ≈ 13 were n (in each group)

5.6. Data collection Methods and Instrumentation

The following procedures were carried out to select the eligible khat chewers for the study, these are; identifying khat sellers, recruitment of khat sellers, and recruitment of khat chewers. The geographic locations of khat sellers to the community were identified through social networking. Heads of the Arba Minch community, and khat chewers were consulted. The locations and time of their opening were listed for randomized selection. Participants were encouraged to ask for clarity if they found it difficult to understand. For data collection, a structured questionnaire that is modified form of World Health organization was used. In addition the World Health Organization Self Reporting Questionnaire (SRQ) format with certain modification was also used for diagnostic purposes. For data collection, a pretested questionnaire pertinent to the study objectives were developed and used. The English version questionnaire was translated into Amharic and distributed to all sampled khat chewers. Medical equipment and materials such as sphygmomanometer (blood pressure cuff) with stethoscope, and glucometer were used to measure the level of physiological and biochemical parameters after and before chewing khat. Four trained nurses were involved in data collection and supervision was carried out by the principal investigator.

5.7. Eligibility

5.7.1. Inclusion Criteria:

The study had been included only adult subjects of Arba Minch town khat chewers aged 18 or above, currently living in the town , regularly chewing khat (at least once per week) over the preceding 12 months.

5.7.2. Exclusion Criteria:

The study had been excluded occasional chewers, smokers, and alcohol drinkers. Khat chewers with temporary residency (visitors, University students) will not been recruited. In addition, khat chewers with mental health problems, hypertensive, diabetics and terminally ill was excluded.

5.8. Standard Operating Procedure (SOP)

5.8.1. Methods of measuring pulse Rate

Pulse: is assessed by palpation (feeling). The middle 3 fingertips are used with moderate pressure for palpation.

Figure 5: *A picture which shows, method of pulse rate evaluation from radial artery.*

5.8.2. Methods of measuring blood pressure

1. First preparing and positioning the participant appropriately

- Make sure that the volunteer has not smoked or ingested caffeine, within 30 minutes prior to measurement
- Position the participant in sitting position. The arm should be slightly flexed with the palm of the hand facing up and the fore arm supported at heart level
- Expose the upper arm
- Wrapping the deflated cuff evenly around the upper arm.
- Apply the center of the bladder directly over the medial aspect of the arm. The bladder inside the cuff must be directly over the artery to be compressed if the reading to be accurate
- Place the lower border of the cuff approximately 2 cm above ante cubital space.

2. For initial examination, performing preliminary palipatory determination of systolic pressure

- Palpate the brachial artery with the finger tips
- Close the valve on the pump by turning the knob clockwise.
- Pump up the cuff until you no longer feel the brachial pulse.

- Note the pressure on sphygmomanometer at which the pulse is no longer felt Release the pressure completely in the cuff, and wait 1 to 2 minutes before making further measurement

3. Positioning the stethoscope appropriately

- Insert the ear attachments of the stethoscope in your ears so that they tilt slightly forward.
- Place the diaphragm of the stethoscope over the brachial pulse; hold the diaphragm with the thumb and index finger.

4. Auscultation of the client's blood pressure

- Pump up the cuff until the sphygmomanometer registers about 30 mm Hg above the point where the brachial pulse disappeared.
- Release the valve on the cuff carefully so that the pressure decreases at the rate 2-3 mmHg per second.
- Deflate the cuff rapidly and completely
- Remove the cuff from the volunteer's arm
- Documentation/ reporting of participant assessment data.

Figure 6: *A picture which shows, blood pressure measurement from Brachial Artery.*

5.8.3. Methods of Measuring Blood glucose level

1. Ask the participant to sit down and explain what you are going to do.

2. Wash your hands and put on gloves

3. Choose the site for the blood sample: usually the side of a finger, but the arm or thigh may be used (change the site used if frequent measurements are needed).

4. Use an alcohol swab to clean the site and let the alcohol dry.

5. Insert the test strip into the monitor, following the instructions. Use a single-use lancet or a lancing device to draw blood and dispose of it in a sharps container.

6. Apply the blood to the testing strip in the correct way: some strips need the blood drop to be over the whole of the test pad and some suck up the blood directly from the site of the bleeding and Place the alcohol swab (note: it will sting) or a piece of gauze over the site and hold it there, or let the patient hold it there until the bleeding stops. Monitor for excess bleeding.

7. Read and record the result, reporting and/or responding to abnormal readings.

8. Tell the patient what the result is, explain it and discuss options.

9. Dispose of all used equipment safely, in line with hospital or health care policies.

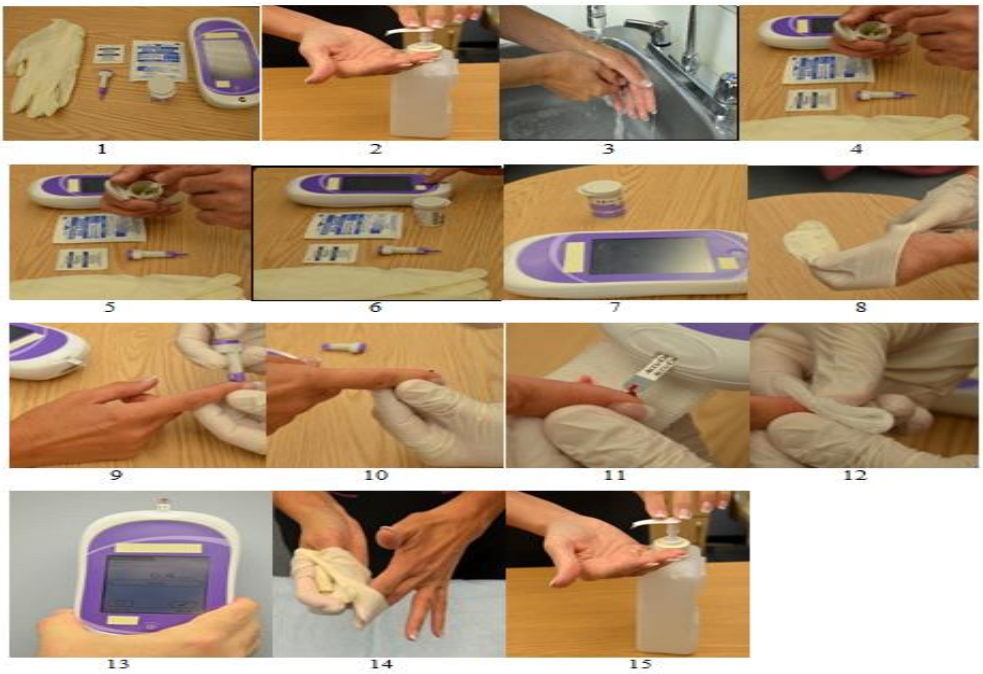

Figure7: *Method and steps of blood glucose concentration measurement by glucometer.*

5.9. Variables of the study

5.9.1. Dependent Variables

- Blood pressure, pulse rate and blood glucose concentration.

5.9.2. Independent Variables

- Age, sex, and marital status, level of education and place of residence.

5.10. Pilot Study

- A pilot study was conducted to determine the optimum amount of Khat consumed by chat chewers and to assure the exact time of chat chewing process takes place.

5.11. Data Quality Control

- Data collectors were trained professionals to insure consistency and to reduce intra and inter observer variation. Close supervision was done by principal investigator throughout the data collection. The collected data were checked for completeness and consistency.

5.12. Operational Definition

- **Addiction:** A physical or psychological craving for higher and higher doses of a drug that leads to bodily harm, social maladjustment, or economic hardship, dependence on a substance, habit, or behavior.

- **Amphetamines:** A class of drugs, similar in some ways to the body's own adrenaline (epinephrine) that act as stimulants to the central nervous system.
- **Cross – Tolerance:** Increased tolerance for one drug that develops as a result of taking another drug
- **Delusions:** Irrational but firmly held beliefs about the word that have basis in reality
- **Euphoria:** Exaggerated sense of happiness and wellbeing brought on by some drugs; popularly called a high.
- **Hallucination:** A sensory perception without external stimuli.
- **Insomnia:** Sleep abnormalities, including difficulty in falling asleep and wakefulness through the night.
- **Stimulants:** Chemical compounds that elevate mood, induce euphoria, increase alertness, reduce fatigue, and, in high doses, produce irritability, anxiety, and a pattern of psychotic behavior. Stimulants include amphetamines, nicotine, caffeine, and cocaine.
- **Substance Induced Psychotic Disorder:** Condition provoked by large, repeated doses of drug, which resembles schizophrenia and includes hallucinations and delusions.
- **Withdrawal Symptoms:** The (usually unpleasant) set of physical symptoms experienced by the user as a result of stopping use of a drug upon which he or she has become dependent; these may include anxiety, insomnia, perspiration, hot flashes, nausea, dehydration, tremors, weakness, dizziness, convulsions, or behavior.
- **Frequent chewers:** those who chew khat for three and more days a week.
- **Less frequent khat chewers:** those who chew khat less than three days a week.
- **Physiological parameters:** are those that specify the work of heart and respiratory system.
- **Levels of physiological parameters:** physiology books state the level of physiological parameters for adult person as follows; systolic and diastolic pressure is 120 and 80mmHg respectively; **breathing rate:**12-16 breath/minute ; body temperature: 37°C; body mass index: <18 kg/m2 underweight, 18-25 kg/m2 normal and 26-30 kg/m2 overweight; heart rate: 60-100beat/minute.
- **Self-rated health status:** is a reliable and valid way of diagnosing patients when compared with physician-reported medical histories.

- **Khat sellers:** those who earning money from chewers by prepared a special place and setup for chewers and sold grams of khat for chewers during khat session.
- **Khat chewing behaviors**: frequency of khat chewing per week, time of the day that spent during khat session, amount of khat chewed within the last 12 months, and grams of khat chewed during khat session.
- **Acute Effect:** Adverse effect (due to exposure to harmful substance) on animal or human, where by severe symptoms develop rapidly and lead quickly to a health crisis. These symptoms often subside when the exposure stops.
- Blood Pressure: the force exerted against blood vessel walls, can be categorized as normal pressure below 120/80 mmHg, elevated systolic blood pressure between 120-129 and diastolic less than 80 mmHg and hypertensive above 130/80 mmHg.
- **Heart Rate:** is the number of beats per minute, with bradycardia less than 60 beats/minute, normal between 60-100 beats/minute and tachycardia over 100 beats/minute.
- **Fasting Blood Sugar:** glucose level is the result of blood samples taken after client fasts for at least eight hours or overnight, with normal level less than 110 mg/dl, IFG between 110- 125 mg/dl and DM over 126 mg/dl.

5.13. Data Analysis

The data collected has been entered on to computer and analyzed using statistical package for social science (SPSS for windows, version 23). Mean, median, range and standard deviation (SD) of data has been calculated by using descriptive statistics. Analysis of variance (ANOVA) was used to check the presence of significant difference in physiological and biochemical parameters of the subjects in a given period of time. The results of the analysis were presented with tables and figures, where appropriate. In all the cases p-value of less than 0.05 was considered as statistically significant.

5.14. Plan for Utilization and Dissemination of result

- The result of the research has been forwarded to responsible bodies like government and private health sectors to upgrade or take action for intervention purpose on how to modify their polices. The outcome of this study may be used by:

A. The Gammo Gofa Zone Health, Labor and Social Affairs.
B. Addis Ababa University, College of Health Science, School of Medicine Department of Physiology and Post Graduate Office.
C. Policy makers to draft rules and regulations about the production, distribution and use of khat.
D. It can also be used as a base line for further research and investigation

5.15. Ethical Clearance

- Ethical clearance for the study was obtained from the Ethics Review Committee of the department of Physiology, Addis Ababa University (AAU). Written consent was obtained from each study participant. The study was not included any invasive procedure which could cause harm to the study participant or to the community. Individuals with high blood pressure, blood glucose, and high pulse rate identified during the study were advised to visit health facilities for confirmation and treatment services.

6. RESULTS

6.1. Socio-demographic characteristics

This community based cross sectional study was conducted to investigate the acute effect of khat edilus on blood pressure, pulse rate and fasting blood sugar. A total of 256 adults were interviewed and blood pressure, pulse rate and blood glucose level was measured, of which 256 participants had completed both the interview and measurements making the response rate of 100 %. Among the 256 study participants, 50 % were chat chewers and 50 % were non-chewers. The majority of participants, 28.9% of khat chewers and 34.1% of the non-chewers were married. Fifty five (43.0%) of khat chewers and 40 (31.3%) of non-chewers had annual income between 10,000 and 50,000 Ethiopian birr. The main religion was Orthodox Christian 39 (30.46%) in khat chewers and 45 (34.9%) in non-chewers. Protestants were 32 (25.0%) and 35 (27.1%) in khat chewers and non-chewers, respectively. A significant number of subjects (61 of khat chewers and 47 of non-chewers) attended modern education, ranging from primary up to tertiary level. The majorities 108 of the khat chewers and 109 of non-chewers were urban residents.

All study participants in both groups were healthy, and no participant reported history of any chronic diseases (hypertension, diabetes mellitus, liver disease, renal disease etc.). No participant in both groups was reported to have the habit of alcohol consumption and cigarette smoking. While the two groups were comparable in most socio-demographic characteristics see *table 6.1 below.*

Table 6.1: Comparison of Socio Demographic Characteristics of Chat Chewers and Non-chewers in Arba Minch town, 2019.

Demographic Variable	***Category***	***Chat-chewers(128)***		***Non-chewers(128)***	
		N=128	***%***	***N=128***	***%***
Sex	**Male**	94	73	76	58.9
	Female	34	27	52	41.1
Marital status	**Married**	57	44.5	64	49.6
	Unmarried	37	28.9	44	34.1
	Divorced	20	15.6	14	10.9
	Widowed	14	10.9	6	5.4
Address	**Urban**	108	84.4	109	85.3
	Rural	20	15.6	19	14.7
Occupation	**Employee**	48	37.5	46	35.7
	Private	15	11.7	19	14.7
	Trade	30	23.4	35	27.1
	Farmer	6	4.7	5	3.9
	Student	15	11.7	16	12.4
	Other	14	10.9	7	6.2
Education status	**Illiterate**	31	24.2	40	31
	Literate	97	75.8	88	69
Education level	**Primary**	15	11.7	25	19.4
	High school	23	18.0	19	14.7
	College	30	23.4	19	14.7
	University	31	24.2	28	20.9
	N/A	29	22.7	39	30.2
Annual income	**None**	16	12.5	28	21.7
	10000-50000	55	43.0	40	31.3
	51000-100000	28	21.87	31	25.1
Religion	**Orthodox**	39	30.46	45	34.9
	Muslim	33	25.7	39	30.2
	Protestant	32	25	35	27.1
	Catholic	11	8.59	6	4.7
	Others	13	10.16	4	3.1
Age	**18-39**	67	52.3	62	48
	31-40	44	34.4	45	35
	41-50	12	9.4	16	13.4
	>50	5	3.9	5	4

6.2. Prevalence of Hypertension, Increased Heart Rate and Diabetes Mellitus

Among participants 4 (3.1%) of khat chewers and 9 (7.0%) of non-chewers have a blood pressure greater than or equal to 140/90 mmHg. Eighteen (14.0%) of chewers and 8 (6.2%) non chewers were diabetic with fasting blood glucose level ≥110 mg/dl. Pulse rate was 17 (13.2%) and 7 (5.4%) in chewers and non-chewers respectively see table 6.2 below

Table 6.2. Prevalence of Hypertension, Increased Heart Rate and Diabetes Mellitus among Study Participants, In Arba Minch Town South Ethiopia.

Variable		*Cases*		*Control*	
		N=128	%	N=128	%
Blood Pressure (mmHg)	**Normotensive**	80	62.0	111	86.0
	Pre-hypertensive	28	21.7	3	2.3
	Hypertensive	16	12.4	6	4.7
	Hypotensive	4	3.1	9	7.0
Pulse Rate (Beats/Minute	**Bradycardia**	13	10.1	18	14.0
	Normal	98	76.0	104	80.6
	Tachycardia	17	13.2	7	5.4
Blood Glucose (mg/dL)	**Hypoglycemic**	3	2.3	8	6.2
	Normal	107	82.9	113	87.6
	Hyperglycemic	18	14.0	8	6.2

6.3. Physiological and Biochemical Measurements

The mean systolic blood pressure and diastolic blood pressure for the chat chewer's were 118.0±16.6 mmHg and 78.8±14.7 mmHg respectively. On the other hand, the mean systolic blood pressure of non-chewers was 112.0±12.1 mmHg and diastolic blood pressure was 78.8±14.7 and 72.9±11.2 mmHg for chewers and non-chewers respectively. Therefore the mean (SBP) systolic blood pressure was significantly higher (P< 0.003) among the chewers than non-chewers, the mean heart rate of the study participants was 77.6±14.8 and 72.9±11.2 chewers and non-chewers respectively. The range of pulse rate of chewers was 49 -109 beats per minutes and 50-104 beats per minutes for non-chewers. The mean fasting sugar level in milligram per deciliter was 97.2 ±21.7 and 88.2±16.8 in chewers and non-chewers respectively.

The range being 50-155 and 50-142 in chewers and non-chewers respectively. The result shown in table 4.3 below demonstrated statistically significant (P=0.003, 0.001) change in the systolic and diastolic blood pressure between two groups. Chat chewers showed significant increase in pulse rate compared to non-chewers (P=0.000).Paired sample t-test showed significant increase in fasting blood sugar among chewers compared to non-chewers

Table 6.3: The Mean Fasting Blood Sugar (FBS) Level (mg/dl), Mean Arterial Blood Pressure (mmHg), Systolic Blood Pressure (mmHg), Diastolic Blood Pressure (mmHg) of Participants; in Arba Minch Town, South Ethiopia.

Variables	Chat-chewers (n=128) M±SD	Control Group (n=128) M±SD	Mean Difference	%	*P*-value
FBS (mg/dl)	**97.2±21.7**	**88.2±16.8**	**9 mg/dl**	**+9.2**	**.000**
SBP (mmHg)	**118.0±16.6**	**112.0±12.1**	**6**	**+5.1**	**.003**
DBP (mmHg)	**78.8±14.7**	**72.9±11.2**	**5.9**	**+7.5**	**.001**
MAP (mmHg)	**90.4± 18.4**	**84.6 ± 15.2**	**5.8**	**+6.2**	**.001**
Pulse Rate	**77.6±34.6**	**72.8±31.887**	**4.8**	**+6.2**	**.000**

*Where: FBS=fasting blood sugar, MAP=mean arterial blood pressure, SBP=systolic blood pressure, DBP=diastolic blood pressure. Values are represented as M ± SD=mean ± standard deviation, % = percentage of change, (+) = Increased from baseline *=statistically significant, **=highly significant (P<0.001), variables statistically significant at P ≤0.05 and P-values were obtained by independent -samples t-test.*

6.4. Chat chewing habit and blood pressure

The overall prevalence of prehypertension and hypertensions for chewers was 28 (21.7%) and 16 (12.4%) respectively, based on ESH classification, 14 (11.2%) had grade I hypertension, 3 (2.4 %) had grade II hypertension and 25 (20 %) pre-hypertensive. The prevalence of prehypertension & hypertension among the non-chewers was 3(2.3%) and 6 (4.7. Based on ESH classification 4(3.2%) had grade I hypertension, 2(1.6 %) had grade II hypertension and 3 (2.4%) pre-hypertensive.

Table 6.4: Comparison of chat chewing habit and blood pressure.

Variable		*Normotensive*		*Pre-hyper tension*		*Hyper tension*		*Hypo tension*	
		N=128	**%**	**N=128**	**%**	**N=128**	**%**	**N=128**	**%**
Chewing frequency	***Every day***	**28**	**21.9**	**9**	**7.0**	**7**	**5.5**	**1**	**.8**
	2-3/week	**27**	**21.1**	**7**	**5.5**	**7**	**5.5**	**3**	**2.3**
	Once/week	**25**	**19.5**	**11**	**8.6**	**1**	**.8**	**0**	**0.0**
	Occasionally	**0**	**0.0**	**1**	**.8**	**1**	**.8**	**0**	**0.0**
Duration of chat chewing	***6 months***	**1**	**.8**	**0**	**0.0**	**1**	**.8**	**0**	**0.0**
	1 year	**16**	**12.5**	**7**	**5.5**	**3**	**2.3**	**2**	**1.6**
	2 years	**23**	**18.0**	**4**	**3.1**	**4**	**3.1**	**0**	**0.0**
	>2 years	**40**	**31.3**	**17**	**13.3**	**8**	**6.3**	**2**	**1.6**

6.5. Chat chewing habit and pulse rate

Pulse rate (beats/minute) of khat chewers group was greater than non-chewers group. There was a higher prevalence of tachycardia 17 (13.3%) among khat chewers group, whereas the majority of participants in the non-chewers group 104 (80.6%) normal pulse rate (beats/min). Independent -samples t-test analysis showed that there was a statistically significant frequency difference between khat chewers and non-chewers group on pulse rate (P= <0.000).

Table 6.5: Comparison of chat chewing habit and Pulse rate.

Variable		*Bradycardia*		*Normal PR*		*Tachycardia*	
		N=13	%	N=98	%	N=17	%
Chewing frequency	***Every day***	4	3.1	34	26.6	7	5.5
	2-3/week	8	6.3	28	21.9	8	6.3
	Once/week	1	.8	34	26.6	2	1.6
	Occasionally	0	0.0	2	1.6	0	0.0
Duration of chat chewing	***6 months***	0	0.0	2	1.6	0	0.0
	1 year	2	1.6	26	20.3	0	0.0
	2 years	3	2.3	25	19.5	3	2.3
	>2 years	8	6.3	45	35.2	14	10.9

6.6. Chat chewing habit and blood glucose concentration

Blood glucose concentration of khat chewers group was greater than non-chewers group. There was a higher prevalence of hyperglycemia 18 (14.1%) among khat chewers group, whereas the majority of participants in the non-chewers group 113 (87.6%) normal blood glucose level. independent -samples t-test analysis showed that there was a statistically significant frequency difference between khat chewers and non-chewers group on pulse rate (P <0.005)

Table 6.6: Comparison of chat chewing habit and Fasting Blood Sugar Level.

Variable		*Hypoglycemia*		*Normal FBG level*		*Hyperglycemia*	
		N=3	**%**	**N=107**	**%**	**N=17**	**%**
Chewing	***Every day***	**0**	**0.0**	**38**	**84.4**	**7**	**15.6**
frequency	***2-3/week***	**2**	**4.5**	**34**	**77.3**	**8**	**18.2**
	Once/week	**1**	**2.7**	**34**	**91.9**	**2**	**5.4**
	Occasionally	**0**	**0.0**	**1**	**50.0**	**1**	**50.0**
	6 months	**0**	**0.0**	**1**	**50.0**	**1**	**50.0**
Duration	***1 year***	**1**	**3.6**	**25**	**89.3**	**2**	**7.1**
of chat	***2 years***	**0**	**0.0**	**29**	**93.5**	**2**	**6.5**
chewing	***>2 years***	**2**	**3.0**	**52**	**77.6**	**13**	**19.4**

6.7. Factors Associated with the Hypertension, Tachycardia and Diabetes mellitus

The multivariate analysis result (Table 6.7) indicated that frequency of khat chewing amount of khat chewing for more than 2 years and 2-3 times per week chewing were statistically significantly affected the level of blood pressure. The multivariate analysis result revealed that the figure of having elevated blood pressure among chewers who chewed 2-3 times per week was three times more compared to who chewed less frequently than it (AOR: 3.88,95% CI: 0.07, 53.8) *table 6.7 below*. Duration of khat chewing for 2 years also have statistically significant effect on pulse rate, the findings shown that, those who chewed khat for two years were 7.38 times more likely to have tachycardia compared to those who have less duration, (AOR :7.38; 95% CI: 1.97-27.6) *table 6.8 below.* The risk of elevated fasting blood glucose level was more than 3.25 times more likely among more than two year chewers compared to who chewed less than or equal to two years (AOR:3.25:95% CI: 0.56-18.9) *table 6.9 below.*

Table 6.7: Multiple linear regression on selected variable for determination of blood pressure, among the Chat chewers

Parameter		Hypertension		COR (95% CI)	AOR (95% CI)	P-value
		Yes (22)	No (235)			
Age in Years	18-30	5	124	1	1	
	31-40	9	80	.527 (.037, 7.530)	1.98 (.15, 26.9)	.637
	41-50	7	22	1.382 (.107, 17.761)	0.76(.06, 9.25)	.804
	≥51	1	9	4.683 (.338, 64.834)	0.26(.02, 9.25)	.250
Marital Status	Married	11	110	1	1	
	Unmarried	4	77	.673 (.118, 3.835)	1.51(.26, 8.47)	.655
	Divorce	3	31	.347 (.053, 2.265)	2.88 (.44, 18.7)	.269
	Widowed	4	17	585 (.072, 4.730)	1.71 (.21, 13.8)	.615
Religion	Orthodox	9	75	1	1	
	Muslim	4	68	.752 (107, 5.29.150)	1.33 (.19, 9.35	.775
	Protestant	6	61	.354 (.043, 2.904)	2.82 (.34, 23.2)	.334
	Catholic	0	17	.973 (.122, 7.738)	.02 (.13, 8.17)	.979
	Others	3	14	.000 (.000)	569134.1 (.00)	.998
Occupation	Government	14	80	1	1	
	Private	1	33	3.000 (.257, 34.987)	0.33 (.03, 3.89)	.381
	Merchant	5	60	.350 (.014, 9.030)	2.86 (.11, 73.9)	.526
	Farmer	0	11	1.914 (.136, 26.981)	0.52 (.04, 7.37)	.631
	Student	1	30	.000 (.000)	368508.1 (.00)	.999
	Others	1	21	2.799 (.156, 50.076)	0.36 (.02, 6.39)	.484
Educational Status	Primary	1	39	1	1	
	Secondary	3	39	.223 (.020, 2.492)	4.49 (.40, 50.3)	.223
	College	8	41	.431 (.071, 2.607)	2.32 (.38, 14.0)	.360
	University	10	48	.606 (.130, 2.824)	1.65 (.35, 7.68)	.524
	NA	0	68	.594 (.134, 2.624)	1.68 (.38, 7.45)	.492
Frequency of Chewing	Everyday	7	54	1	1	
	2-3/weeks	13	144	.533 (.019, 15.267)	3.88 (.07, 53.8)	.013*
	Once/week	1	36	.418 (.016, 10.826)	2.39 (.09, 62.0)	.599
	Occasionally	1	1	.087 (.002, 3.635)	11.5 (.27, 481)	.200
Duration of Chewing	6 months	3	12	1	1	
	1 year	7	137	1.590 (.233, 10.825)	0.63 (.09, 4.28)	.636
	2 year	4	27	.282 (.062, 1.286)	3.55 (.78, 16.2)	.102
	≥2 year	8	59	1.454 (.288, 7.349)	0.69 (.14, 3.48)	.041

*Where: COR=crude odd ratio; AOR=Adjusted Odd Ratio * = statistically significant, Variables statistically significant at p <0.05.*

Table 6.8: Multiple linear regression on selected variable for determination of pulse rate among the Chat chewers.

Parameter		Tachycardia		COR (95% CI)	AOR (95% CI)	P-value
		Yes (24)	No (233)			
Age in Years	18-30	12	117	1	1	
	31-40	10	79	.436 (.03, 6.80)	2.29 (.15, 35.8)	.553
	41-50	1	28	.725 (.04, 11.6)	1.38 (.09, 22.0)	.820
	≥51	1	9	.24 (.01, 7.69)	4.24(.13,138.2)	.417
Marital Status	Married	12	109	1	1	
	Unmarried	7	74	2.22 (.21, 23.3)	.45 (.04, 4.74)	.507
	Divorce	3	31	2.58 (.23, 28.9)	.39 (.03, 4.33)	.441
	Widowed	2	19	2.25 (.17, 29.1)	.44 (.03, 5.75)	.534
Religion	Orthodox	4	80	1	1	
	Muslim	12	60	1.30 (.12, 14.7)	.77 (.07, 8.65)	.830
	Protestant	5	62	1.30 (.12, 14.7)	.13 (.01, 1.41)	.093
	Catholic	1	16	7.70 (.71, 83.8)	.32 (.03, 3.64)	.362
	Others	2	15	3.08 (.27, 34.4)	1.09 (.04, 29.6)	.959
Occupation	Government	9	85	1	1	
	Private	4	30	1.22 (.12, 12.7)	.82 (.08, 8.54)	.867
	Merchant	7	58	1.84 (.15, 22.5)	.54 (.04, 6.65)	.634
	Farmer	1	10	1.47 (.14, 15.8)	.68 (.06, 7.33)	.751
	Student	2	29	1.91 (.08, 45.7)	.52 (.02, 12.5)	.689
	Others	1	21	.99 (.06, 15.5)	1.00 (.06, 15.5)	.998
Educational Status	Primary	6	34	1	1	
	Secondary	4	38	5.56 (.85, 36.3)	.18 (.03, 1.18)	.073
	College	6	43	5.95 (.91,39.1)	.19 (.03, 1.10)	.063
	University	6	52	5.37 (.80, 35.9)	.19 (.03, 1.24)	.083
	NA	2	66	3.95 (.62, 25.2)	.25 (.04, 1.62)	.147
Duration of Chewing	6 months	1	14	1	1	
	1 year	7	137	.43 (.04, 4.9)	2.33 (.20, 27.03)	.499
	2 year	3	28	.13 (.04, .507)	7.38 (1.97, 27.6)	.003*
	≥2 year	13	54	.47 (.09, 2.41)	2.14 (.41, 11.0)	.363

*Where: COR=crude odd ratio; AOR=Adjusted Odd Ratio * = statistically significant, Variables statistically significant at p <0.05.*

Table 6.9: Multiple linear regression on selected variable for determination of blood glucose concentration among the Chat chewers.

Parameter		*Hyperglycemia*		*COR (95% CI)*	*AOR (95% CI)*	*P-value*
		Yes (26)	**No (231)**			
Age in Years	**18-30**	**11**	118	1	1	
	31-40	**9**	80	.31 (.05, 1.85)	3.35 (.58,)19.4	.198
	41-50	**3**	26	.30 (.05, 1.87)	3.49 (.57, 21.4)	.197
	≥51	**3**	7	.29 (.03, 2.36)	4.19 (.52, 34.1)	.247
Marital Status	**Married**	**12**	109	1	1	
	Unmarried	**4**	77	.84 (.16, 4.28)	1.49 (.34, 6.58)	.830
	Divorce	**6**	28	.48 (.07, 3.09)	2.89 (.53, 15.8)	.440
	Widowed	**4**	17	1.54 (.26, 9.28)	.83 (.163, 4.23)	.636
Religion	**Orthodox**	**10**	74	1	1	
	Muslim	**6**	66	.81 (.13, 5.19)	1.45 (.28, 7.63)	.825
	Protestant	**6**	61	.44 (.06, 3.14)	2.86 (.49, 16.7)	.412
	Catholic	**1**	16	1.10 (.16, 7.59)	1.07 (.18, 6.24)	.922
	Others	**3**	14	.26 (.01, 4.43)	4.00 (.26, 60.9	.352
Occupation	**Government**	**10**	84	1	1	
	Private	**5**	29	3.43 (.29, 39.4)	.24 (.02, 2.79)	.323
	Merchant	**8**	57	5.23 (.42, 64.5)	.16 (.01, 1.97)	.199
	Farmer	**0**	11	5.48 (.45, 66.1)	.15 (.01, 1.81)	.181
	Student	**2**	29	.000 (.000)	63561266.651	.999
	Others	**1**	21	3.29 (.19, 57.3)	.26 (.02, 4.42)	.413
Educational Status	**Primary**	**3**	37	1	1	
	Secondary	**6**	36	.69 (.14, 3.48)	1.29 (.28, 6.01)	.661
	College	**4**	45	1.19 (.29, 4.91)	.91 (.23, 3.59)	.801
	University	**7**	51	.78 (.17, 3.53)	1.41 (.32, 6.27)	.748
	NA	**6**	62	.59 (.13, 2.54)	1.91 (.45, 8.03)	.475
Frequency of Chewing	**Everyday**	**7**	54	1	1	
	2-3/weeks	**16**	141	.24 (.01. 6.39)	5.74 (.22, 150.9)	.395
	Once/week	**2**	35	.26 (.01, 6.55)	5.33 (.22, 130.1)	.413
	Occasionally	**1**	1	.09 (.003, 3.2)	15.3 (.47, 491.9)	.192
Duration of Chewing	**6 months**	**2**	13	1	1	
	1 year	**9**	135	.49 (.07, 3.34)	2.88 (.44, 18.7)	.466
	2 year	**2**	29	.24 (.07, .84)	4.86 (1.43, 16.5)	.190
	≥2 year	**13**	54	.33 (.05, 1.93)	3.25 (.56, 18.9)	.011*

*Where: COR=crude odd ratio; AOR=Adjusted Odd Ratio * = statistically significant, Variables statistically significant at p <0.05.*

7. DISCUSSION

Catha edulis (Khat) leaves are used by millions of people as a social habit, and there is little information about its biological activity (Carvalho, 2003). Moreover, biological effects of khat are inadequately investigated and controversial (Dimba *et al.,* 2004). In this work, the khat chewers showed a significant increase in blood pressure, pulse rate and blood glucose level. In addition to its socio-economic burden, cathinone can cause multiple health problems. Cathinone is similar in structure and pharmacological activity to amphetamine (Motarreb *et al.,* 2010). D-amphetamine is known to exert different forms of hepatotoxicity in-vivo and in-vitro when tested on hepatocytes. Khat is expected to cause similar toxic effects on the liver but the available data are few and sporadic (Vitcheva *et al.,* 2010).

Khat Chewing and Blood Pressure: This study compared mean systolic, diastolic and mean arterial blood pressure between adults in Arba Minch town who are Khat chewers and non-chewers. We demonstrated the association of Khat chewing with increased mean systolic, diastolic and mean arterial blood pressure, which suggests that Cathinone may have a more unfavorable effect on blood pressure. Earlier studies have also suggested that chronic use of Khat predisposes to high blood pressure (Fikru *et al*., 2006; Tesfaye *et al.*,2008; Workineh *et al.,* 2010).

Our study suggests, using a comparative study design that long-term Khat chewing contributes to an increase in blood pressure at the population level. As shown in the table 6.4 present finding confirms an earlier report of association between Khat chewing and elevated blood pressure from a cross sectional study in a similar population (Tesfaye *et al.*,2008).

A similar cross sectional study by Workineh et al (Workineh *et al.,* 2010), who recruited 660 participants between the age of 35-65 years showed a significantly higher diastolic blood pressure among chat chewers than non-chewers. However, no significant difference was observed in their mean systolic blood pressure. This observation in case of diastolic blood pressure is in agreement with the findings of the present study. Similarly another study conducted in Addis Ababa (Fikru *et al*., 2006), showed that mean diastolic pressures was higher in participants who have been chewing khat than non-chewers.

A cross-sectional study in Bahir Dar, North west Ethiopia (Bizuayehu and Muluken, 2014) Khat (Catha edulis) chewing on blood pressure, revealed that systolic blood pressure was significantly higher among khat chewers than matched controls. The result of this study regarding increase in SBP was in agreement with the current study. Similar study conducted in Butajira between chewers and non-chewers, the result showed statistically significant increase in SBP and DBP of khat chewers than non-chewers (Tesfaye *et al.,* 2008).

The concomitant use of other classical cardiovascular risk factors, such as smoking, alcohol, or dietary salt intake along with Khat may modify the extent of association between Khat chewing and blood pressure (Motarreb *et al.,* 2010). However, as indicated in Table 6.7, our regression analysis revealed that frequent chewing behaviors was significantly associated with raise in blood pressure. Thus, the significant differences in mean blood pressure and prevalence of sub-optimal blood pressure, we demonstrated in this study are unlikely to be confounded by the behavioral characteristics. Although the specific mechanism is yet to be understood, the effect on blood pressure in our study population may be explained by the peripheral vasoconstrictor effect of Cathinone (Chapman *et al.*, 2010), which may be sustained in regular Khat chewers. The mean systolic, diastolic and mean arterial blood pressures of Khat chewers in this study were significantly higher than that of non-chewers, ($p < 0.05$).

Khat Chewing and Pulse Rate: Findings from the present study demonstrated that khat chewers had significant increase in heart rate, when compared to control groups (*Table 6.3).* The mean heart rate in khat chewers was 77.6±34.6 beats per minutes (+6.2%). This is in agreement with an experimental study performed on 22 study subjects in Debre Markos North Ethiopia, which was aimed to investigate electrical activities of the heart using Biopac measurement before and after stimulation by chewing khat, revealed increased heart rate after chewing (Etenesh, 2014). Similarly study (Nageeb *et al.,* 2000) designed to investigate the effect of khat chewing on blood pressure and heart rate, revealed that there exists significant increase heart rate among chewers compared with the non-chewers. A similar experimental crossover study, 33ml placebo juices or 33ml juices + 45g ground khat leaves (3-months study) revealed increased heart rate, which is in consistent with this study (Sallam *et al.* 2016).

However Toennes and his colleagues have found that no change in heart rate was found in their study. It is noted that tolerance develops to these sympathomimetic effects in chronic users

(Toennes *et al.,* 2003). The existing literature does not provide a clear picture of the mechanism of khat chewing related to increased pulse rate. Earlier studies have showed that khat chewing increases heart rate among chewers. Recent studies also highlighted that the fact that frequent chewing is related to increase heart rate. The substances present in khat (cathinone and Cathine) have tendency to increase sympathetic effects then, SA node fires more than the intrinsic firing rate. Heart rate is greater than the intrinsic heart rate (Widler *et al.,* 1994; Jeffrey and Goldberger, 1999; Toennes *et al.,* 2003;) so heart rate increment among chewers was associated with sympathetic stimulation by substances present in khat then, SA node fires more than the intrinsic firing rate.

Fasting Blood Glucose Level and Khat Chewing: Diabetes mellitus is a major public health problem in the world. The number of patients with diabetes is increasing due to population growth, aging, urbanization, and increasing prevalence of obesity and physical inactivity (Kamalakkanan., 2003). The finding from the present study suggests that FBS level of khat chewers was higher when compared to the controls. However, it still remained in the normal range for almost all users. Similar finding was reported in Yemen (Butheinah *et al.,* 1990) on the effect of habitual khat chewing on glycemic control, body mass index. The study showed that khat chewing by patients with type 2 diabetes is likely associated with poor glycemic control, than controls. Similar study conducted in Sana'a, Yemen (A. Alsalahi *et al.,* 2015) on the effect of *Catha edulis* (khat) on pancreatic functions in streptozotocin-induced diabetes, also showed that serum fasting blood sugar level was significantly increased in cases compared to controls. The low dose of khat contributed to exacerbation of hyperglycemia by provoking further destruction of pancreatic β-cells, which emphasized the direct *in vitro* cytotoxicity of khat in pancreatic β-cells. A similar longitudinal study conducted in Egypt (Ibrahem *et al.,* 2012), revealed that khat chewing resulting in additional adverse effects to type 2 diabetes patients by increasing insulin resistance due to increased resistin levels and its cathinone-induced catecholamine secretion, leading to increased FBG.

Unlike the finding of the present study, a cohort study conducted in Addis Ababa, Ethiopia (Demeke *et al*., 2016), showed that acute effects of crude extract of *Catha edulis* possessed significant hypoglycemic properties in normal and STZ induced type 2 diabetic rats. This finding was supported by a study (Ashenafi and Ephrem, 2017), indicate that khat at higher doses could produce anti-diabetic effect, the effect being expressed without hypoglycemia.

This discrepancy could be due to the difference in protocol, the age difference employed by the prior and present studies. Furthermore the difference in food habits and life styles may contribute to this discrepancy. The glycemic activity of khat has not yet been elucidated. Khat main constituent cathinone is structurally similar to nor-ephedrine and has a similar mechanism of action like amphetamine, through releasing catecholamine from pre-synaptic storage sites. It increases ACTH hormone levels through stimulation of β-adrenergic receptors by its amphetamine-like effect and inhibits insulin release due to induced nor-adrenaline and activation of pancreatic α2-adrenoceptors by the released catecholamine, the indirect sympathetic effect of khat may act as insulin antagonist (Saif-Ali *et al* 2003; Al-Motarreb *et al*., 2010).

8. CONCLUSION

In summary we studied the acute effect of khat chewing in blood pressure, pulse rate and blood glucose concentration in adult's subjects of Arbaminch, Southern Ethiopia. Particularly, we already compared the blood pressure of chewers with non-chewers, pulse rate of chewers with non-chewers and the blood glucose level of chewers with non-chewers. The result shows that Khat chewing induced changes in carbohydrate metabolism, manifested by high fasting blood sugar level. Furthermore, Khat chewers showed a significant change in blood pressure compared to non-chewers, which indicates khat chewing did have unfavorable effects on blood pressure, and significant increase in heart rate compared with the non-chewers. In addition, the study shows that, there was high prevalence of hypertension, tachycardia and hyperglycemia in Arbaminch town chat chewers, and it conform that there is a hidden epidemic in this population. We believe that this study can be used as a reference line for further studies such as, for governmental and non-governmental concerned bodies.

9. RECOMMENDATIONS

Based on the results of the present study, we recommend for further study the following:

- It is necessary that policy maker and health care provider should continuously conduct periodical survey for screening and early detection, treatment, and control for cardiovascular system and metabolic abnormalities like, hypertension, tachycardia and hyperglycemia in communities.

- Since people with hypertension and hyperglycemia may or may not exhibit any symptoms, their high blood pressure is often undiagnosed until complications occur. Hence, regular blood pressure, pulse rate and blood glucose concentration screening can facilitate early diagnosis and treatment and reduce the risk of further complications associated with hypertension and hyperglycemia.

- Health extension workers, health center and hospital professionals must have to participate on prevention, management of hypertension and hyperglycemia through community education, counseling, perform the initial evaluation and set up a care plan that includes primary and secondary prevention strategies.

- Therefore, provision of sustainable health education to the community about adverse effects of chat chewing and prevention of cardiovascular and metabolic abnormalities is highly recommended.

- Appropriate counseling on lifestyle, including aerobic exercise, minimum of 30 minutes/5 days/week and diet control as necessary guidelines to prevent cardiovascular risk and excessive weight gain.

- The present study is a cross sectional in design, further longitudinal study (cohort in design) with larger sample size is needed to be conducted to evaluate whether the changes in FBS level, BP, increase in heart rate indeed are associated with khat chewing.

10. STRENGTH AND LIMITATION OF THE STUDY

Strength of the study:

Pretest was done

The data was primary

During the study time, health education was given by the principal investigator for each of the study participant about blood pressure, pulse rate and blood glucose abnormalities.

Limitation of the study:

No mechanism was designed to counter check the reported age or chat chewing behavior.

The effect of other contributing factors and associated health problems such as diabetes, kidney diseases, heart diseases, level of cholesterol, were not assessed by laboratory but included in the questioner.

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12. ANNEXES

Annex I

የጥናቱ ተሳታፊዎች የመረጃ ቅጽ

ስሜ ቴዎድሮስ ፋንታዬ ይባላል፡፡

በአዲስ አበባ ዩኒቨርሲቲ ህክምና ፋኩሊቲ ፊዚዮሎጂ ትምህርት ክፍል የድህረምረቃ ተማሪ ስሆን የመመረቂያ ፅሁፌን በጫት ዙሪያ ለመስራት ወስኛለሁ፡፡ እርሰዎም በዚህ ጥናት ላይ በመሳተፍ የበኩልዎን አስተዋጽኦ እንዲያበረክቱ ተጋብዘዋል፡፡

ውድ የጥናቱ ተሳታፊዎች በጥናቱ ያልዎትን ተሳትፎ ለመወሰን የሚከተሉትን ማብራርያ ያድምጡ/ይመልከቱ፡፡

1. **የጥናቱ ዓላማ፡- የዚህ ጥናት ዓላማ ጫት አዘውትረው የሚቅሙ ሰዎችን ደም ግፊት፣ በደም ውስጥ የስኳር መጠን ፣የልብ ምትና የአተነፋፈስ ስርዓት መለካትና ልዩነት ማወቅ፡፡**
2. **አጠቃቀም፡-እርስዎ ጫት ከመቃምዎ በፊት የልብ ምት፣አተነፋፈስ ፣የስኳርመጠንና የደምግፊት ይለካሉ፡፡**
3. **ሊደርስ የሚችል አደጋ፡- ምንም የለም፡፡**
4. **ከጥናቱ የሚገኝ ጥቅም፡- በዚህ ጥናት ተሳታፊ በመሆንዎ ጫት መቃም ያለውን ውጤት ያውቃሉ፡፡**
5. **ሚስጥራዊነት፡-የማንኛውም የጥናቱ ተሳታፊ መረጃ በሚስጥር ይያዛል፡፡**
6. **ፈቃደኝነት፡-እርስዎ በጥናቱ ለመሳተፍ ፈቃደኛ ያለመሆን፣ ማንኛውም መረጃ እና ናሙና ያለመስጠት እንዲሁም ጥናቱን በማንኛውም ጊዜ የማቋረጥ መብትዎ የተጠበቀ ነው፡፡**
   - **ጥናቱን በተመለከተ ማንኛውም ጥያቄ ካለዎት የዋናው ተመራማሪ አድራሻ፡-**
   - ✓ **ቴዎድሮስ ፋንታዬ**
   - ✓ **አዲስ አበባ ዩኒቨርሲቲ**
   - ✓ **ህክምና ፋኩሊቲ ህክምና ፊዚዮሎጂ ትምህርት ክፍል**
   - ✓ **ስልክ** +25191028702

Annex II

PARTICIPANT INFORMATION SHEET

Title of the project:

Study of acute effect of Catha Edulis (khat) on blood pressure, pulse rate, and blood glucose in adults in Arba Minch, Ethiopia.

Principal Investigator: Tewodros Fantaye

Supervisor: Wendyefraw Mekonin (PHD)

Coordinating office: Addis Ababa University, School of Medicine, and Department of Physiology Purpose: The objective of this research is to study acute effect of khat chewing and its effect on Blood pressure, blood glucose, respiratory rate and Pulse Rate. This research undertaking is for partial fulfilment of the requirements for the Master Degree in Medical Physiology.

Procedure and Participation: You will be asked for measuring your Blood pressure, Respiratory rate, and blood glucose and pulse rate before chewing khat.

Confidentiality: The use of information for any purpose other than that to which participants consented is unethical to the participants. The information you provide is not disclosed in the way it identified your personal characteristics and privacy.

Risk: The proposed research does not have any inhumane treatment of research participants and any physical harm, social discrimination, psychological trauma and economic loss.

Freedom to withdraw: If you want to participate in the study, you have full right to with draw from the study any time you wish.

Person to Contact: The participant has the right to ask information that is not clear about the research context and content before and or during the research work. You can contact the principal investigator and supervisor.

Principal Investigator name and address: Tewodros Fantaye (BSc), Department of Physiology, College of Health Sciences, Addis Ababa University, Mobile: +251910287028

Supervisor name and address: Wendyifraw Mekonin (PhD), Department of Physiology, College of Health Sciences, Addis Ababa University.

Annex III

የጥናቱ ተሳታፊዎች የስምምነት ቅጽ

- የጥናቱ ተሳታፊ መለያ ቁጥር_____
- ጥናቱን በተመለከተ በቂ ማብራሪያ ተደርጎልኛል፡፡ የጥናቱን ዓላማ በሚገባ የተረዳሁ ሲሆን በጤንነት ላይ ምንም አይነት ጉዳት እንደማያደርስ እና ሚስጥር እንደሚጠብቁ ስለተገነዘብኩ በጥናቱ ለመሳተፍ መወሰኔን በፊርማዬ አረጋግጣለሁ፡፡
- የጥናቱ ተሳታፊ ስም_____
- ፊርማ_____
- ቀን_____
- የመረጃ ሰብሳቢው ስም_____
- ፊርማ_____
- ቀን_____

Annex IV

Consent Form

Code No._____

- Information about the study has been explained formed by the investigator. I have understood that the objective of the study is to assess the acute effect of khat on Blood pressure, blood glucose, respiratory rate and pulse rate. This will not hurt my health. It has also explained to me that I have the right to stop. Participation at any time between and there is nothing I will lose if I refuse to participate.
- I agree to participate in the study and here by approve my agreement with my signature

participant signature _____Date_____

Investigator's signature_____Date _____

Annex V

በአማርኛ የተዘጋጀ ቃለ መጠይቅ

ክፍል አንድ

<u>መመሪያ</u>፡- ይህ ፎርማት በአጠቃላይ 26 ጥያቄዎችን የያዘ ሲሆን ጥያቄዎቹም የጥናቱ አላማ የሚመለከቱ ጥያቄዎች ናቸው፡፡ በታቻለዎ መጠን በጥንቃቄ ባዶ ቦታዎችን በመሙላት እና ከተሰጡት አማራጮች ውስጥ ተገቢ የሆኑትን መልሶች በማክበብ ሁሉንም ጥያቄዎች እንዲመልሱ ይጠየቃሉ፡፡

I. **የመለያ ጥያቄዎች**

➢**የመለያ ቁጥር**_____**ቀን፡** _____

1.**አድራሻ፡ ሀ. ገጠር ለ. ከተማ**

➢ **ቀበሌ፡**_____**ወረዳ**_____**የቤት ቁጥር፡** _____

2.**የትውልድ ቦታ፡** _____

II. **የማህበራዊ እና ስነ ህዝብ ባህሪያት**

3.**እድሜ፡**_____

4.**ፆታ፡ ሀ. ወንድ ለ. ሴት**

5.**የጋብቻ ሁኔታ፡ ሀ. ያገባ ለ. ያላገባ**

ሐ. የተፋታ መ. ባለቤቱ/ቷ የሞተችበት/የሞተባት

6.**ሀይማኖት ሀ. ኦርቶዶክስ ለ. ሙስሊም ሐ. ፕሮቴስታንት**

መ. ካቶሊክ ሠ. ሌላ (ይግለፁት) _____

7.**ስራ ሀ. ተቀጣሪ ለ. የግልሰራተና ሐ. ንግድ**

መ. ገበሬ ሠ. ተማሪ ረ. ሌላ (ይግለጹት)_____

8.**ብሔረሰብ**

9.**አመታዊ ገቢ**_____

10. **የትምህርት ደረጃ ሀ. ያልተማረ ለ. የተማረ**

I. **አንደኛ ደረጃ ያጠናቀቀ** II. **ሁለተኛ ደረጃ ያጠናቀቀ**

III. 12+3 IV. 12+4

III. ዝርዝር ጥያቄዎች

1.ጫት የመቃም ልምድ አለህን? ሀ. አዎ ለ.የለኝም

2.መልስዎ አዎ ከሆነ ምን ያህል?

ሀ. በየተቀኑ ለ. በሳምንት ከ3 እስከ 2 ቀናት

ሐ. በሳምንት አንድ ጊዜ መ. አልፎ አልፎ

3.ምን አይነት ጫት ነው የሚቅሙት?

ሀ. ጊዶሌ ለ. ኮንሶ ሐ. በለጨ መ.ሌላ_____

4.በአንድ ጊዜ የምን ያህል ብር ጫት ነው የሚቅሙት?

ሀ. ከ 10-20 ብር ለ. 30-50 ብር ሐ.ከ50-100 ብር መ. ከ100 ብር በላይ

5.ለምን ያህል ጊዜ ጫት ቅመዋል?

ሀ. ለ6 ወራት ለ.ለ1አመት ሐ.ለ2 አመታት መ. ከ2 አመት በላይ

6.አብዛኛውን ጊዜ ከማን ጋር ነው የሚቅሙት?

ሀ. ብቻየን ለ. ከባለቤትዎ ጋር ሐ. ከጓደኛዎ ጋር መ.ከወላጅዎ ጋር

7.ለምንድን ነው ጫት የሚቅሙት?

ሀ. ለመዝናናት ለ. ጠንክሮ ለመስራት ሐ. ለመጸለይ መ. ትርፍ ጊዜዬን ለመግደል ሠ. ድብርት ለማስወገድ ረ. ደስ የማይል ስሜትን ለማስወገድ

ሰ. ማህበራዊ ጉዳይ ስለሆነ ሸ. ሌላ ምክንያት (ይግለፁ) _____

8.በአሁኑ ወቅት ጫት በሚቅሙት ጊዜ ሲጋራ ያጨሳሉን?

ሀ. አዎ (መልስዎ አዎ ከሆነ ወደ ጥያቄ ቁጥር 20 ይሂዱ) ለ.አይደለም

9.አዘውትረው የሚጠቀሙት የትንባሆ አይነት የትኛው ነው?

ሀ. ሲጋራ ለ. ሽሻ ሐ. ሲጋራ እና ሽሻ መ. ሌላ_____

10. ጫት ከቃሙ በኋላ አልኮል ይጠጣሉን? ሀ. አዎን ለ. አይደለም

11. መልስዎ አዎ ከሆነ ለምን?

ሀ. እንቅልፍ እንዲወስደኝ ለ. ድብርትን ወይም ደስ የማይል ስሜትን ለማስወገድ

ሐ.ደስታን ለመጨመር መ. ደስታዬን ለማቆየት

12. ጫት ሲቅሙ ምን አይነት ስሜት ይሰማዎታል?

ሀ. የደስታ ስሜት ለ. ከጭንቀት ነጻ የመሆን ስሜት

ሐ. ድብርት ረ. ብስጭት ሰ. የአእምሮ መነቃቃት (ንቁ መሆን) ጥንካሬ

ሸ. የራስ ምታት

13. ጫት ከቃሙ በኋላ ምን አይነት ስሜት ይሰማዎታል?

ሀ.ድብርት ለ. ብስጭት ሐ. ከፍተኛ የሆነ ጭንቀት

መ. የደስታ ስሜት ሠ. የመዝናት ስሜት ረ. የምግብ መዘጋት ሰ. አትኩሮት

ሸ. ከፍተኛ የሆነ ሀሳብ ቀ. የራስ ምታት በ. የሆድ ድርቀት

14. ጫት ሳትቅም ስትቀር ደስ የማይል ስሜት ይሰማሃልን? ሀ. አዎ ለ. አይሰማኝም

15. በህክምና ተረጋግጦ ክትትል የሚያደርጉት በሽታ አለብዎት? ሀ. አለ ለ. የለም

16. መልስዎ አዎ ከሆነ ይግለጹት ምን? ከመች ጀምሮ_____

ክፍል ሁለት፡ በጫት ላይ የመመርኮዝ ደረጃ ከፍተኛነት

ባለፉት 12 ወራት፤

1. የእርስዎ ጫት የመቃም ባህሪ ከቁጥጥር ውጭ እየወጣ ሄድዋል ብለው አስበው ያውቃሉን?

በፍጹም ወይም ደግሞ በፍፁም ሊባል የሚችል	አልፎአልፎ	ብዙውንጊዜ	ሁል ጊዜ ወይም ሁልጊዜ ሊባል በሚቸል

2. ጫት መቃምን ማቆም ሲያስቡ ያናድዎታልን ወይም ያሳስቦታል?

በፍጹም ወይም ደግሞ በፍፁም ሊባል የሚችል	አልፎአልፎ	ብዙውንጊዜ	ሁል ጊዜ ወይም ሁልጊዜ ሊባል በሚቸል

3. ጫት ቃሚ በመሆንዎ አሳሳቢ ይሆንብዎታልን?

በፍጹም ወይም ደግሞ በፍፁም ሊባል የሚችል	አልፎአልፎ	ብዙውንጊዜ	ሁል ጊዜ ወይም ሁልጊዜ ሊባል በሚቸል

4. ጫት መቃምን ለማቆም ተመኝተው ያውቃሉን (አልታክዘን)?

በፍጹም ወይም ደግሞ በፍፁም ሊባል የሚችል	አልፎአልፎ	ብዙውንጊዜ	ሁል ጊዜ ወይም ሁልጊዜ ሊባል በሚቸል

5. ጫት መቃምን ለማቆም ወይም ደግሞ ጫት ሳይቅሙ ለመንቀሳቀስ ምን ያህል አስቸጋሪ ሆኖ አግኝተውታልን?

በፍጹም ወይም ደግሞ በፍፁም ሊባል የሚችል	አልፎአልፎ	ብዙውንጊዜ	ሁል ጊዜ ወይም ሁልጊዜ ሊባል በሚቸል

Annex VI

ENGLISH QUESTIONNAIRE

Part –I

Instructions: This format contains a total of 23 questions, which are pertinent to the research objectives. You are kindly requested to answer all as completely as possible and carefully by filling the blank spaces and encircling one appropriate choice from the alternatives given.

I. Identification

1. Code number of the subject: _____Date_____

2. Address: a. Rural b. Urban

II. Socio demographic characters

3. Age_____

4. Sex a. Male b. Female

5. Marital status: a. married b. unmarried c. divorced d. widowed

6. Religion: a. Orthodox b. Muslim c. Protestant d. catholic e. others (specify)_____

7. Occupation: a. employee b. unemployed c. trade

d. farmer e. student f. Others (specify)___

8. Ethnicity _____

9. Education level: a. an Illiterate b. Literate

I. Elementary school complete II. High school complete

II. Completed College IV. University degree and above

III. Specific questions

10. Do you have a habit of khat chewing? a. Yes b. No

11. If yes, how often?

a. Every day b. 3-2 days per week c. once a week d. occasionally

12. How much you chew at a time per cost in birr?

a. 10-20 birr b. 30-50 birr

c. 50-100 birr d. >100birr

13. For how long have you been chewing khat?

a) 6 months b) 1 year

c) 2 years d) > 2 years

14. With whom do you usually chew khat?

a. alone b. with spouse

c. with friend's d. parents

15. Why do you chew khat?

a. for relaxation b. to increase performance

c. for praying d. to kill extra time

e. to avoid depression f. to avoid unpleasant feelings

g. for socialization h. other reasons (specify) _____

16. Do you use tobacco currently during khat chewing?

a. Yes (If yes go to Q. 20) b. No

17. Were you ever in life a regular user of the following tobacco products?

a. Cigarettes c. Cigarettes and Shisha

b. Shisha d. Other _____

18. Do you take alcohol? a. Yes b. No

19. What do you feel during you chew khat?

a. happiness e. frequent urination

b. euphoria f. irritability

c .tension relief g. mental alertness/wakeful/strength

d. depression h. head ache

20. What do you feel after you chew khat?

a. Depression e. Relaxation i. Head ache

b. Irritability f. Suppressed appetite j. Constipation

c. Insomnia g. Concentration

d. Happiness h. Facilitated thinking

21. Do you feel unpleasant symptoms when you are not chew khat? a. Yes b. No

22. Do you have diagnosed illness in the past? a. Yes b. No

23. If yes, specify _____

Part II. Severity of Dependence on Khat

In the last 12 months,

1) Did you ever think that your khat chewing was out of control?

Never or almost never	Sometimes	Often	Always or nearly always

2) Did the prospect of not chewing any khat make you anxious or worried?

Never or almost never	Sometimes	Often	Always or nearly always

3) Did you worry about your khat chewing?

Never or almost never	Sometimes	Often	Always or nearly always

4) Did you wish you could stop chewing khat?

Never or almost never	Sometimes	Often	Always or nearly always

5) How difficult would you find it to stop or go without khat chewing?

Not difficult	**Quite difficult**	**Very difficult**	**Impossible**

PHYSIOLOGICAL AND BIOCHEMICAL MEASURMENTS

A-BLOOD PRESSURE _____

B-PULSE RATE_____

C-BLOOD GLUCOSE CONCENTRATION_____