#### What can research evidence tell us about:

# Effect of khat on health and society; Rapid Evidence Review [Feb 2021]

#### Key message

Khat chewing increases the risk of oral problems and raises blood pressure and heart rate which are established risk factors for cardiovascular disorders. Beside these, the burden of Khat chewing goes beyond the Khat chewers; affecting women, children, families and communities at large.

### Summary of the review

- Khat chewing was highly associated with elevated Blood pressure(BP) and heart rate which are established risk factors for cardiovascular diseases.
- Khat induced a very consistent and reproducible type of cell death in humans but evidence have not found on the direct relationship between khat and cancer
- Sub-chronic exposure to khat affects short-term memory depending on the duration of exposure. However, it does not have any effect on long-term memory. Khat induces neurobehavioral changes.
- There are high socioeconomic implications of Khat chewing including big money spending on buying Khat, getting forced into credit and money borrowing.
- The social burden of Khat chewing goes beyond the Khat chewers affecting women, children, families and communities at large.

#### Implications for policy & practice and research

- Even though the qualities of evidence included in this review range from inconclusive, low and medium; it can be considered that Khat chewing results in varieties of health consequences. Therefore this review is thought to be sufficient to regulate Khat from its production to consumption.
- The social and economic effects of khat consumption on individual and household need further research.

#### What is Rapid evidence Review?

Rapid evidence review addresses the needs of policymakers and managers for research evidence that has been appraised and contextualized to a specific context in a matter of hours or days. This rapid evidence review goes beyond research evidence and integrates multiple types and levels of evidence

# Where did this Rapid Evidence Review come from?

This document was developed in response to the request from Khat Research Advisory Task Force established with an intention to look for research evidence to advice the khat regulation drafting team. It was prepared by the Knowledge Translation Directorate and Health System Research Directorate, Ethiopian Public Health Institute.

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- Key findings from research findings

• Recommendations







# 1. Introduction

#### **1.1 Background**

Khat is defined as a shrub (Catha edulis) of the "staff-tree" family that is cultivated in the Middle East and Africa for its leaves and buds which are the source of a habituating stimulant when chewed or used as a tea (Kalix, 1992a). According to Peter Kalix who is a toxicologist, Cathinone is an alkaloid that has been discovered in the leaves of khat. Cathinone, was soon found to have a pharmacological profile closely resembling that of amphetamine (Kalix, 1992b).

An estimated 20 million people worldwide use khat on a regular basis as a stimulant (Elmenyar, Mekkodathil, & Al-thani, 2015). Various literature reviews indicate that khat grows in East Africa and in southern Arabian Peninsula. The inhabitants of these regions frequently chew khat. Historical references to the chewing of khat leaves is for their euphoric and stimulant effect which dates back many centuries and today this practice is prevalent in such countries: Somalia, Yemen, Kenya, and Ethiopia (Capriola, 2013; Kalix, 1992b; WHO, 1980).

Khat is known by a variety of names, including: Abyssinian tea, African salad, bushman's tea, catha, chat, flower of paradise, gat, herari, jaad, kaad, leaf of Allah, mirra, qaat, qat, and tea of the Arabs among others. The earliest scientific report on khat was written in the 18th century by the botanist Peter Forskal. Many believe that khat originated in Ethiopia, from where it spread to the hillsides of east Africa and Yemen; others argue that it originated in Yemen before spreading to Ethiopia and nearby countries (Lamina, 2010)

#### **1.2 Burden of Khat-Chewing in Ethiopia**

Khat is native to the eastern and southern regions of Africa but is grown extensively as a cash crop in Ethiopia, where it is freely available and is a highly valued export commodity (El-menyar et al., 2015; Lamina, n.d.). As per the 2019/20 report from the National Bank of Ethiopia, Khat is the third in its export share with 10.9% following coffee and flower recording a share of 28.6% and 14.1% respectively (NBE, 2020).

Though there are no concrete data on how many people consume khat in Ethiopia, national NCD STEPS survey which was done in 2015 indicated that about 15.8% were khat users, of which, 21.1.% of men and 9.4 % of women (EPHI, 2015). In recognition of the khat chewing burden, the Ministry of Health (Ethiopia) established the national task

force to advise the khat regulating legislation drafting team through generating synthesized evidence on effect of khat on health.

Based on the request made, the team at the Knowledge Translation Directorate, EPHI, conducted preliminary electronic database search if evidence was readily available. However, the team didn't find systematically and transparently reviewed evidence. Therefore, this rapid evidence review has become a necessity to be prepared.

# 2. Objectives of the review

This rapid evidence review aims to identify and summarize the best available evidence on effect of khat on health and society.

# 3. Methods

A rapid evidence review approach (adapted from SURE guide for Rapid Response Services) was applied to search, appraise and summarize the best available evidence on the effect of khat on health. We identified the PICO with respect to the objective of the review to facilitate searching of relevant articles.

# 3.1 PICO

Population: Human population regardless of age and sex
Intervention (exposure): Khat or Catha edulis use
Comparator: non-users of khat
Outcome: Health effect (any)

#### 3.2 Inclusion criteria

The following criteria were used to include articles in this review.

Study Design: Systematic reviews, and clinical trials.

**Context (setting)**: Global studies were considered without restriction to any geographical context.

#### 3.3 Exclusion criteria

The following criteria were used to exclude articles in this review.

- Reviews which are not systematic and transparent (e.g. literature reviews)
- Cross-sectional studies
- In vivo and in vitro experiments
- Case series/case report

- Expert opinions and editorials
- Studies published other than English language
- Studies with no free full texts
- Studies with synthetic cathinone which resembles Khat effect
- Studies conducted with additional interventions like alcohol and tobacco

### 3.4 Search strategy:

To answer the question under review we searched for high quality studies (systematic reviews & RCT) from the following international data bases: SUPPORT Summaries, Health Systems Evidence, Epistemonikos, PDQ-Evidence, the Cochrane Library, and PubMed. The searching was made with no date or no language restriction. The last search was made on January 11, 2021.

**PubMed:** Khat\* [tw] OR Catha edulis [tw] OR Chat [tw] OR "Substance abuse\*" [tw] OR "Abyssinian tea" [tw] OR "African salad" [tw] OR "bushman's tea" [tw] OR Catha [tw] OR chat [tw] OR "flower of paradise" [tw] OR gat [tw] OR jaad [tw] OR kaad [tw] OR "leaf of Allah" [tw] OR mirra [tw] OR qaat [tw] OR qat [tw] OR "tea of the Arabs" [tw] OR "Natural amphetamine" [tw] OR stimulant [tw] OR "nervous system stimulant" cathinone [tw] OR "qat leaves" [TW] OR "Catha" [Mesh] OR "cathinone" [Supplementary Concept]

Cochrane Library: Khat or Catha edulis

Epistemonikos: khat or Catha edulis Google Scholar: "Khat"

# 4. Review findings

Based on the search strategy we found a total of 1350 studies from PubMed, Cochrane Epistemonikos and Google scholar. Using the eligibility criteria 13 articles were reviewed and summarized (9 systematic reviews and 3 randomized clinical trials). Summarization of the evidence was done under the following themes: effect of khat on: oral health; cardiovascular; genetic health and malignancy; physiological and metabolic effects, and neurology. We have also included the findings for social and economic aspects of khat consumption and presented separately at the end of this document.

# 2.1 Effect of khat on oral health

We found two highly relevant systematic reviews and one experimental study that assessed effect of khat on oral health and key findings are as follows.

# Key Findings:

• Based on the systematic review study entitled "The association of khat (catha edulis) chewing and orodental health", khat chewing increased the odds of the respective oral problems such as mucosal white lesions, gum recession, periodontal pocketing and gum bleeding (Kalakonda, Ijaz, & Gamal, 2017). While

literature on the topic is scarce, there is a need for generation of more quality evidence.

- According to the experimental study which followed a group of chewers and nonchewers for 20 days, Khat chewing is associated with lower Plaque Index (PI) scores; however, differences were only significant at day 20. The observed antiplaque and anti-gingivitis properties indicate that khat chewing is probably not detrimental to the periodontium. The validity of previous findings supporting an opposite view is undermined by lack of control for confounders, particularly smoking (Al-hebshi & Al-ak'hali, 2010).
- According to the systematic review titled 'Is khat (catha edulis) chewing a risk factor for periodontal diseases?' Most of the studies exhibited a positive correlation between khat chewing and periodontal disease. Accordingly, the analysis of the evidence reveals that khat chewing is destructive to the periodontium and enhances the risk of periodontal disease progression(Astatkie, Demissie, & Berhane, 2014). However, due to variability of studies, more longitudinal case-controlled studies are highly warranted to establish a causal relation between khat chewing and periodontal disease.

#### 2.2 Effect of khat on cardiovascular health

#### **Key Findings:**

We found two highly relevant systematic reviews that assessed the effect of khat on cardiovascular health and key findings are as follow:

#### **Key Findings:**

- The systematic review and meta-analysis by Kalkidan et al to establish epidemiological association between khat chewing as exposure (potential risk factor) and hypertension as an outcome, found out that there is no statistically significant association of khat chewing as an epidemiological risk factor for hypertension (Hassen et al., 2012). However, this conclusion is subject to a small number of studies with cross sectional study design. Thus, there is a need for a robust studies on khat as an epidemiologic risk factor for hypertension considering further aspects of chewing, like dose-response, duration of chewing and coexistence of other co-morbid factors of hypertension.
- To establish whether there is a risk factor for cardiovascular disorder from khat chewing a systematic review and Meta-analysis was conducted in 2017. Based on the findings, khat chewing was highly associated with elevated Blood Presure and heart rate which are established risk factors for cardiovascular diseases (A.Teshale & Nikodimos, 2017)

#### 2.3 Effect of khat on genetic health & malignancy

We found one highly relevant systematic reviews and one experimental study that assessed the effect of khat on genetic health and malignancy and key findings are as follow:

### **Key Findings:**

- In an experimental study conducted by EAO Dimba et. al, a standardized organic extract of khat induced a very consistent and reproducible type of cell death in various human leukemia cell lines and in peripheral human blood leukocytes. The potential mechanism(s) for khat-induced apoptosis in human leukaemic cells is unknown; however, the results on khat-induced apoptosis point to an activation of the extrinsic cell death pathway (Onyango, Fossan, & Costea, 2004).
- A systematic review by Zx chonge et al evaluated the use of khat (catha edulis) as a risk factor for cancer. The pooled analysis from the systematic review did not find a direct relationship between khat and cancer but anti-cancer effect would require to be proofed on human studies (Chong, Ho, Yan, & Alshagga, 2020).

#### 2.4 Effect of khat on physiological and metabolic health

We found one systematic review & meta-analysis and one experimental crossover study conducted at the Substance Abuse Research Centre in Jazan University, Saudi Arabia which assessed the effect of khat on physiological and metabolic health and key findings are as follow:

#### **Key Findings:**

- Khat showed a clear enhancing effect on physical performance. Cathine/cathinone act as stimulants to increase the capacity to perform exercise. Thus, khat produces the same effects which leads to banning of amphetamine (Sallam, Sheikh, Baxendale, Azam, & El-Setouhy, 2016)
- A systematic review & meta-analysis by Alsalahi et.al in 2016 found out that it was difficult to draw a meaningful conclusion with respect to the glycemic effect of Catha Edulis since the meta-analysis results were insignificant with high heterogeneity among subgroups and are greatly conflicting (Alsalahi et al., 2016).

#### 2.5 The effect of khat on neurological health

We found two highly relevant systematic reviews that assessed the effect of khat on neurological health and key findings are as follow:

#### Key Findings:

- According to the systematic review titled "Toxic effect of khat (Catha edulis) on memory" the effect of acute, and subchronic exposure to khat showed that short-term memory appears to be affected depending on the duration of exposure. However, it did not show effect on long-term memory (Berihu et al., 2017).
- According to the systematic review titled 'Effect of khat (Catha edulis Foresk) on Neurobehavioral functions it suggested that there were significant difference between khat exposed and control group for the neurobehavioral changes. Although a number of studies regarding the topic is limited, there is the high quality of evidenced that khat (Catha edulis) induced neurobehavioral changes (Berihu & Asfeha, 2015).

#### Socio Economic Effect of khat utilization

#### A/ Effect of khat on society

A systematic review conducted by Mihretu on problematic Khat use found the following:

The key finding from this systematic Review is as follows:

- Problematic khat use constitutes, but is not limited to, harms, increased use over time, and frequent engagement in other psychoactive substances misuse.
- Khat use is different from problematic khat use since it is occasional and used for prayer, social, and functional reasons.
- Strong empirical studies that could establish thresholds for patterns of problematic khat use and a culturally suitable problematic khat use measures that follows a bottom-up approach of scale development are warranted (Mihretu, Nhunzvi, Fekadu, Norton, & Teferra, 2019).

A primary study in Ethiopia by Yeraswork Admassie (Admassie, 2017) indicated as the impact of khat chewing extends beyond the khat chewers themselves involving women, children and the entire community.

#### B/ Economic implications of khat consumptions

• The authors of this rapid review were not able to retrieve valuable and high level evidence (systematic reviews and or RCT) with regard to the effects of khat consumptions on the economy of individuals, households of a country or region. From the outset the reviewers thus call for setting this aspect of khat a future research agenda in which renowned caliber of economists participate. To pave the way for further high level global and regional decisions via robust research in this perspective, we have hereafter tried to summarize what has been written on economic aspects of khat consumption whether that evidence is in the form of written books or article of any type. The key findings of the Included articles are as follow:

- A study from Kenya found that Khat consumption was widely accepted by all age groups and that the number of days Khat was consumed, the variety of Khat consumed, highest level of education attained by the consumer, employment status and income had negative effects on the household economy. There was a significant association between household economy and marital status as well as employment status. Khat regulation was preferred as well as community sensitization on the implication of Khat consumption (Omar, Kennedy, & Mbugua, 2019).
- A descriptive study from Somalia indicated that on the average, users chewed over 250g of khat per day, spending an average of USD 7.29. Severalscholars have argued that if Somalia did not import khat, the country would be one of the most socioeconomically developed countries in Africa. The country would save millions of dollars every day, people who work would contribute their full income to their families, and there would be greater impact on work performance in the areas that promote economic growth. The overall health of the nation would also be improved, further improving socio-economic conditions in Somalia (Yassin & Ali, 2018).
- A study conducted in northern part of Ethiopia found out that khat chewers who
  participated in the study spent at least 500 ETB on khat per week even though more
  than half of the respondents were unwilling to disclose khat expenditure. Most khat
  chewers drank alcohol after chewing khat and smoked cigarette and consumed
  substances such as peanut, coffee and soft drinks while practicing khat chewing
  (Eticha, Kahsay, Ali, & Gebretsadik, 2016).

The other more comprehensive study involving multiple sites was conducted in Ethiopia by Yeraswork Admassie. This study is both descriptive and qualitative including the experiences of Khat chewers in rehabilitation center as a consequences of Khat chewing and its addictive nature (Admassie, 2017). According to this study:

- There is an escalating consumption/addiction and impacts of khat both in areas where a study is conducted (Assosa and Harari) and beyond in the country.
- Khat addicts and heavy users often access their khat supply through a vicious cycle of credit, credit payment, and back to credit, supplemented by cash-on hand purchase with borrowed money that is followed by the uphill struggle to settle that debt, thereby ruining their household economy and shaming their family.
- The social impact of khat chewing extends beyond the khat chewers themselves involving women, children and the entire community.

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# **Conflicts of interest**

No conflicting of interest.

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