

USE OF KHAT AND ASSOCIATED SUBSTANCES DURING COVID-19 PANDEMIC: POTENTIAL ADVERSE CONSEQUENCES

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ABSTRACT

The epidemic of COVID-19 has become a major public health challenge globally. There are concerns that an increased number of individuals who abuse substances could encounter greater risks of experiencing the effects of COVID-19. The present paper reviews the potential health risks that can be associated with using the commonly abused stimulant plant, khat and associated substances during the COVID-19 pandemic. The literature indicates that khat chewing, as practiced by most chewers, can facilitate SARS-CoV-2 virus transmission and spread. Chewers with compromised health due to khat could be at greater risks of being affected by COVID-19, and these effects may include worsening of respiratory, cardiovascular, CNS, renal, gastrointestinal, hepatic, hemostatic and immune dysfunctions. Furthermore, tobacco smoking and alcohol drinking in association with khat use has the potential to intensify most of these disorders. The review suggests that healthcare providers and khat chewers should take appropriate precautionary measures when khat and/or the associated substances are used during COVID-19 epidemic. The research community should also conduct further studies to provide additional and more specific information on the topic.

Keywords: COVID-19; coronavirus; khat; tobacco; alcohol; drug abuse

INTRODUCTION

Since the end of 2019, the world has encountered a pandemic of a novel coronavirus disease 2019 (COVID-19) which

has cast a major threat to public health worldwide. With no effective treatment and slow vaccine development, the virus has caused millions of infections and deaths globally (McIntosh, 2020; Meng

et al., 2020; World Health Organization, 2020a; Yuki et al., 2020). So far, the primary approach for handling COVID-19 has been to control viral infection and preform recovery care for affected individuals. As an infectious disease, COVID-19 causes symptoms that can vary in severity of illness, depending upon such factors as viral load, duration of infection and condition of the patient. Although COVID-19 is considered a respiratory disease, the symptoms diagnosed include multiple illnesses, which are described below under background. Conditions that mimic or enhance these symptoms have the potential to worsen the effects of COVID-19. In this regard, some classes of abused psychoactive substances are reported to produce overlapping effects with those caused by COVID-19, thereby worsening the outcomes (Dubey et al., 2020; Nishiga et al., 2020; Vital Strategies, 2020; Volkow, 2020; Wang et al., 2020; Wei & Shah, 2020). While the commonly reported such substances include opioids, alcohol, tobacco/nicotine, amphetamines, marijuana/cannabis and cocaine, others with the potential to cause similar effects remain to be identified and reviewed.

OBJECTIVE AND METHOD

The present paper reviews the potential consequences of interactions between COVID-19 and the widely abused stimulant plant drug, khat (*Catha edulis*) and substances commonly used in association with it (Abebe, 2013; Abebe, 2014; Cox & Rampes, 2003; Odenwald & Al-Absi, 2017; World Health Organization, 2006). This review is the first of its kind and has the potential to provide useful

information for healthcare providers, khat chewers and researchers. Most of the information was collected by systematically searching articles written in English in PubMed, Medline, Scopus, and Google Scholar databases until December 2020. Search terms used were COVID-19, SARS-CoV-2, pandemic, infection, epidemiology, pathogenesis, disease, transmission, diagnosis, treatment, khat, *Catha edulis*, alcohol, cigarette smoking, substance abuse, substance misuse, substance use disorders, addiction, adverse health effect, and adverse interaction. Full texts of relevant cross references were retrieved from the search results. Other available scientific literature and recommendations were also accessed in authoritative books and in the WHO and CDC websites. Some leading newspaper reports related to COVID-19 and substance use have been added where deemed appropriate. Excluded in the review were case reports, duplicate studies, corresponding pieces, and retracted papers.

BACKGROUND

SARS-CoV-2 transmission and symptoms of COVID-19

In humans, SARS-CoV-2 is transmitted mostly from person to person by direct or indirect contact. Accordingly, people who are in close proximity/contact with COVID-19 patients are at higher risks for getting viral infection (Nishiga et al., 2020; Wei & Shah, 2020). In a newly infected person, SARS-CoV-2 requires binding to angiotensin converting enzyme 2 (ACE2) receptor in order to enter a host cell. Once inside, the virus hijacks the cell's machinery and makes innumerable copies of itself, which then invades other cells

to continue the cycle. As the virus multiplies, an infected person may shed abundant amounts of it, particularly during the first week or so (McIntosh, 2019; Meng et al., 2020; Nishiga et al., 2020; Yuki et al., 2020; Wei & Shah, 2020).

Whereas the severity of COVID-19 illness can range from mild to severe/critical, the symptoms developed in most cases are the consequences of host immune reactions to the presence of the virus. These reactions may include multiple target cells and steps, and are manifested by different responses, mainly involving inflammatory reactions. In rare cases, the immune response becomes overzealous and may result in what is known as cytokine storm, with massive inflammatory

reactions that can potentially be life-threatening. However, most patients with COVID-19 represent only mild cases (Hussain et al., 2020; McIntosh, 2019; Meng et al., 2020; Nishiga et al., 2020; Yuki et al., 2020; Wei & Shah, 2020).

In Table 1 are listed the commonly reported effects of COVID-19 on various organs/systems under different levels of severity (Garland et al., 2020; Hussain et al., 2020; McIntosh, 2019; Meng et al., 2020; Nishiga et al., 2020; Yuki et al., 2020;; Wei & Shah, 2020). It should be noted that while the nature and intensity of the effects can vary with the severity of the disease, there are also overlapping effects among the various categories. From the information in the table, the respiratory

Table 1. Summary of commonly reported effects of COVID-19 on various organ systems under different levels of severity. Note that while the nature and intensity of the effects observed can vary with the severity of the disease, there are also many cases of overlapping effects (see references in text)

Severity of Disease	Effects
Mild	Respiratory <ul style="list-style-type: none"> Mild pneumonia (majority), cough (dry), sore throat, runny nose (congestion), sneezing Gastrointestinal <ul style="list-style-type: none"> Gastritis, nausea, vomiting, abdominal pain, diarrhoea Others (brain/CNS, muscle) <ul style="list-style-type: none"> Fever, fatigue, headache, myalgia, loss of smell and/or taste
Moderate	Respiratory <ul style="list-style-type: none"> Pneumonia with frequent fever and cough, shortness of breath (difficulty in breathing), tachypnoea (mainly in children)
Severe/critical	Respiratory <ul style="list-style-type: none"> Pneumonia with hypoxia, dyspnoea, tachypnoea, respiratory distress/acute respiratory distress syndrome, pulmonary edema, persistent pressure in chest, respiratory impairment Cardiovascular <ul style="list-style-type: none"> Shock (septic), myocardial inflammation/injury, heart failure, plummeting blood pressure, coagulopathy/blood clotting Brain (CNS) <ul style="list-style-type: none"> Encephalopathy/inflammation, confusion, stroke, seizures Others <ul style="list-style-type: none"> Metabolic abnormalities, high fever, acute kidney injury/failure, liver damage, other organ dysfunctions, conjunctivitis/inflammation

effect of COVID-19 is more prominent, while its other effects appear to be less consistent and these include the gastrointestinal (GI), cardiovascular (CV), nervous/brain, renal, hepatic, immune and hematologic/hemostatic dysfunctions (Garland et al., 2020; McIntosh, 2019; Meng et al., 2020; Nishiga et al., 2020; Yuki et al., 2020; Wei & Shah, 2020).

Epidemiology of khat use and associated practices

Khat is a psychoactive shrub *predominantly* grown and used in East Africa and the Arabian Peninsula regions (Abebe, 2013, Abebe, 2014, Cox & Rampes, 2003; Odenwald & Al-Absi, 2017; World Health Organization, 2008). More recently, its use has expanded to other surrounding and far flung places including Europe, North America and Australia (Abebe, 2018; Ageely, 2008; Al-Hebshi, 2005; Odenwald & Al-Absi, 2017). The fresh leaves of khat are commonly chewed for recreational, medical, event celebration and several other purposes, primarily due to their stimulant and euphoric effects. Globally, over 20 million people are estimated to be habitual khat chewers (Abebe, 2018; Cox & Rampes, 2003; Odenwald & Al-Absi, 2017; World Health Organization, 2008).

During the past several decades, there has been a consistent rise in the use of khat in most places. Previous studies in East Africa and Yemen have reported a use prevalence ranging from 30% to 90% (Abebe, 2014; Abebe, 2018; World Health Organization, 2008). In most cases, habitual chewers consume khat almost every day (4-6 hours) for many years, as long as 20 or so years. Consequently, the practice of khat chewing is considered a public health concern, not only

locally but also nationally, regionally, and even internationally (Abebe, 2018; World Health Organization, 2008).

The leaves of khat are typically chewed without much of a concern for cleanness and contamination safety. Every step involved in the harvesting, packaging, transport and delivery of khat could be associated with viral exposure risks (Ageely, 2008; Hassan, 2018). In almost all cases, khat chewing is also an intimate communal activity (usually involving 6-20 people) that creates fertile ground for viral transmission and spread. In such settings, tobacco is also smoked from cigarettes and waterpipes which are often shared among chewers, potentially serving as media of SARS-CoV-2 transmission (Ageely, 2008; Hassan, 2018).

Besides smoking tobacco along with khat chewing, some chewers also indulge in heavy drinking of alcoholic beverages after khat sessions to terminate the stimulant (insomnia) effect of the herb. This behavior thus makes these khat chewers vulnerable to the additional effects of alcohol (Abebe, 2014; Abebe, 2018).

With regard to the use of other substances with khat, the literature indicates that khat serves as a gateway drug to others, more commonly to nicotine/tobacco and alcohol. Another possible reason for combination use is previous exposure to these substances before starting chewing khat (Abebe, 2014; Ageely, 2008; Al-Maweri, 2017).

Medical effects of khat and associated substances

Fresh leaves of khat contain a number of bioactive compounds, and of these, cathinone, cathine and tannins contribute to their major effects (Abebe, 2014;

Ageely, 2008; Al-Motarreb, 2010). While both cathinone and cathine produce central and sympathetic stimulation and euphoria, cathinone is by far more potent. Being structurally related to amphetamine, cathinone has similar effects as amphetamine (Abebe, 2014; Abebe; Ageely, 2008; Al-Motarreb, 2010; Dhafalah & Santavy, 2004).

The effect of cathinone on brain's dopaminergic pathways is linked to the euphoric effect of khat (Abebe, 2014; Abebe, 2018; Ageely, 2008; Al-Maweri et al., 2018; Odenwald & Absi, 2017). This effect is associated with moderate psychological dependence without clear physical dependence. However, physical dependence of khat can be important in susceptible individuals. Signs of withdrawal are also reported with discontinuation of khat after chronic use. Coupled with the psychological dependence, the withdrawal effects could be one more reason for continued use of khat. Tolerance to khat has also been documented (Abebe, 2018). Overall, due to its central nervous system (CNS) stimulation, depending upon several other factors, khat consumption may also result in anxiety, aggression, insomnia, anorexia, malaise, depression, mania, psychotic reactions, and hallucinations. Peripherally, the sympathomimetic effect of khat causes stimulation of certain target organs, such as the heart and blood vessels, while inhibiting others like the gastrointestinal (GI) system.

Tannins in khat produce major adverse effects as astringents in the GI tract and oral cavity, and the effects on the GI tract further slows its motility, thereby contributing to khat's constipating effect (Abebe, 2018; Al-Alimi et al., 2017; Al-Motarreb, et al., 2010; Ridder et al, 2007; Staurung et

al., 2018). Tannins also cause hepatotoxicity, and at high enough concentrations they can promote blood coagulation and thrombus formation (Al-Alimi et al., 2017; Alkadi et al., 2008; Staurung et al., 2018).

Some constituents of khat, especially flavonoids and polyphenols at high concentrations, have been shown to be pro-inflammatory (Naji et al., 2015) and this effect, together with those of tannins, are linked to free radical generation (Kennedy et al., 2020). These mechanisms of action are implicated in khat-induced oral and GI cancer.

Resulting from its central anorexic and GI effects, khat has the potential to cause nutritional deficiency. These effects, together with khat's direct immunomodulatory activity, play a role in the weakening of the immune system, predisposing chewers to increased susceptibility to infectious diseases, such as TB (Abebe, 2018; Al-Motarreb et al., 2010; Alvi et al., 2015; Hassan, 2018; Ketema et al., 2015; Naji, et al., 2015; The Economist, 2018). The adverse effects of khat on other organ systems, such as the respiratory system and kidneys, are linked to such multidimensional factors as free radical generation, inflammation and circulatory dysfunctions induced by khat components (Alvi et al., 2015; Ketema et al., 2015; Naji, et al., 2015; Woldeamanuel & Geta, 2019; Al-Mamary et al., 2002).

Table 2 summarizes the effects of khat that are potentially linked to the symptoms of COVID-19 listed in Table 1.

As noted above, the use of khat is associated with heavy consumption of tobacco/nicotine and/or alcohol. The effects of these substances on the human body are amply discussed in the literature, and broadly these include adverse effects the

Table 2. Summary of commonly reported relevant effects of khat chewing on various organ systems. Note that while the nature and intensity of effects can vary with the amount of khat chewed, the duration of chewing and the condition of the chewer, most of the short- or intermediate-term effects may persist during the long-term consumption of the herb (see references in text)

Systems Affected	Effects Produced
Central nervous system	<p>Short/intermediate-term effects</p> <ul style="list-style-type: none"> Mild euphoria, excitement, alertness, insomnia, talkativeness, lethargy, depression, headache/migraine, psychotic reaction (high doses), hallucinations, inability to concentrate, irritability, fine tremor and depression (post-khat use), anorexia, nausea and vomiting, polydipsia, hyperthermia, perspiration <p>Long-term effects</p> <ul style="list-style-type: none"> Psychosis, depressive reactions, impaired cognitive functioning, increased tremor, seizures, withdrawal effect
Respiratory system	<p>Short/intermediate-term effects</p> <ul style="list-style-type: none"> Tachypnea <p>Long-term effects</p> <ul style="list-style-type: none"> Pulmonary edema, bronchitis
Cardiovascular system and kidneys	<p>Short/intermediate-term effects</p> <ul style="list-style-type: none"> Tachycardia/palpitation, arrhythmia, vasoconstriction, increased blood pressure Procoagulant <p>Long-term effects</p> <ul style="list-style-type: none"> Increased cardiovascular disorders, myocardial infarction, heart attack, cerebral haemorrhage/stroke Urinary retention, kidney damage
Gastrointestinal and hepatic system	<p>Short/intermediate-term effects</p> <ul style="list-style-type: none"> Gastrointestinal inhibition, constipation, gastritis <p>Long-term effects</p> <ul style="list-style-type: none"> Upper gastrointestinal disorders (eg., stomach/duodenal inflammation, irritation, ulcers, reduced nutrient absorption), severe constipation, risk for upper gastrointestinal tumours, haemorrhoids, liver cirrhosis/hepatotoxicity, liver cancer and liver fibrosis
Oro-dental effects	<p>Short/intermediate-term effects</p> <ul style="list-style-type: none"> Dry mouth, oro-dental lesions (eg., dry mouth, caries, periodontal diseases), multiple other moderate oral disorders <p>Long-term effects</p> <ul style="list-style-type: none"> Severe oro-dental disorders; oral mucosal keratosis, oral cancer
Metabolic and endocrine systems	<p>Long-term effects</p> <ul style="list-style-type: none"> Multiple hormonal disorders, malnutrition, weight loss, hyperglycemia
Inflammation, oxidative stress, immune modulation	<p>Short/intermediate-term effects</p> <ul style="list-style-type: none"> Antiinflammatory <p>Long-term effects</p> <ul style="list-style-type: none"> Proinflammatory, oxidative damage Immune modulation

cardiovascular, CNS, respiratory, and hepato-intestinal systems. Additionally, both substances cause nutrient deficiencies

and immune suppression by different mechanisms (Abebe, 2014; Abebe, 2018; Wang et al., 2020; Wei & Shah, 2020).

USE OF KHAT AND ASSOCIATED SUBSTANCES AS RISK FACTORS FOR INCREASED SARS-COV-2 EXPOSURE AND COVID-19 COMPLICATIONS

Increased risk for SARS-CoV-2 exposure and transmission

SARS-CoV-2 is a highly contagious virus which is mostly transmitted from person to person by direct or indirect contact (Hassan, 2018; Meng et al., 2020; McIntosh, 2020; Yuki et al., 2020). As mentioned earlier, khat chewing is likely to increase exposure to the virus by either one of the ways or both ways (Ageely, 2008). In this regard, besides the role of khat per se, tobacco smoking can be a contributory factor during khat session. Related to this problem, it is documented that khat chewing is commonly associated with the spread of TB among Somali chewers (Hassan, 2018).

Moreover, khat and alcohol, due to their CNS effects, can cause altered thoughts and judgements of chewers, potentially making them less concerned about self-protection. In addition, all the three substances chewers consume can inhibit the immune system, particularly with chronic use, further predisposing the chewers to greater susceptibility to viral infection (Abebe, 2013; Abebe, 2014; Sopor, 2002; Watson & Darban, 1988).

INCREASED RISK FOR COVID-19 COMPLICATIONS

Respiratory disorders

COVID-19 is considered to be a respiratory disease, although it also affects different other organs. Normally, relatively a small amount of khat is not expected to produce toxic effects on the respiratory system. However, with prolonged use,

it can cause respiratory disorders that may be manifested by conditions such as tachypnea, pulmonary edema, bronchitis and pneumonia (Cox & Rampes, 2003; Woldeamanuel and Geta, 2019). Since the majority of khat chewers are chronic consumers, these effects provide added challenge to the respiratory health of COVID-19 patients who chew khat, putting them at a higher risk of respiratory/pulmonary abnormalities. Consistent with this, similar respiratory problems have been reported with amphetamine and methamphetamine (Canadian Center on Substance Use and Addiction, 2020; Dubey et al., 2020; Vital Strategies, 2020; Volkow, 2020).

Respiratory problem that might be caused by tobacco smoking by khat chewers could be another issue for consideration (Dubey et al., 2020; Volkow, 2020). Tobacco smoking has previously been shown to diminish the ability of the lungs to respond to SARS-CoV-2 infection and increase fatality rates in COVID-19 patients (Wang et al., 2020a; Wong et al., 2020b; Wei & Shah, 2020). It is thus reasonable to expect that the damaging effect of tobacco smoking on the respiratory system can even be greater if patients also chew khat. However, alcohol consumption per se has not been reported to have significant respiratory effects.

Cardiovascular (CV) disorders

Among patients with the risk of becoming severely ill with COVID-19 are those with CV issues, which can be worsened by chronic khat use as noted above (Abebe, 2018; Ageely, 2008; Ali et al., 2010; Alkadi et al., 2008; Cox & Rampes, 2003; Mozes, 2011). The effect of khat on the CV system is multifactorial, and this includes increased blood pressure, pulmonary

hypertension, cardiac hyperactivity, arrhythmias, coronary artery diseases and even heart failure. Such CV conditions being also caused by a severe form of COVID-19, khat chewing is likely to aggravate them (Dubey et al., 2020; Meng et al., 2010; McIntosh, 2020; Vital Strategies, 2020; Volkow, 2020; Yuki et al., 2020). Being associated with CV adverse effects, tobacco smoking and alcohol consumption by khat chewers can also have the potential to intensify the CV disorders caused by both khat and COVID-19 (Dubey et al., 2020; Vital Strategies, 2020; Volkow, 2020; Wang et al., 2020a; Wei & Shah, 2020; World Health Organization, 2020b).

Central nervous system (CNS) disorders

As part of its multiple overlapping effects that involve neuronal, hormonal and circulatory mechanisms, chronic khat consumption can result in generalized CNS effects manifested by stimulation, confusion, fatigue, and depression, hallucinations, psychosis, and even stroke, among others, (Abebe, 2014; Abebe, 2018; Ageely, 2008; Ali, et al., 2010; Moses, 2011). As with methamphetamine, there is a high possibility that at least some of these effects can exacerbate those of COVID-19 (Dubey et al., 2020; Vital Strategies, 2020; Volkow, 2020). The CNS effects of tobacco and/or alcohol are also likely to cause even a more severe state of mental disturbances with khat and COVID-19, although the mechanism is unclear (Dubey et al., 2020; Volkow, 2020; Wang et al., 2020b; Wei & Shah, 2020; World Health Organization, 2020b; World Health Organization, 2020c).

Kidney damage

It has been reported that in susceptible individuals, prolonged khat consumption

can cause kidney damage in different forms (Cox & Rampes, 2003; Kennedy et al., 2020). This effect has the potential to worsen the abnormal conditions of the kidneys that occur in severe COVID-19 (Dubey et al., 2020; McIntosh, 2020; Yuki et al., 2020). While the effect of tobacco smoking on the kidneys is insignificant, chronic alcohol use has also been reported to result in changes in kidney function as manifested by impairment of sodium handling, and fluid and blood filtration (Epstein, 1997). This effect of alcohol can cause further damage to kidneys already affected by khat and COVID-19.

Gastrointestinal (GI) disorders

While constipation, as a major GI effects of khat, does not seem to relate to COVID-19, there are concerns that other GI effects of the shrub can intensify at least some of the common GI effects of COVID-19. In this respect, among other things, khat has been reported to cause gastritis, gastric ulcers, and even upper GI tumors/malignancy in some chewers (Abebe, 2018; Al-Alimi et al., 2017; Cox & Rampes, 2003; Odenwald & Al-Absi, 2017). These effects of khat can enhance the overlapping GI effects caused by COVID-19 shown in Table 2 (Dubey et al., 2020; Wei & Shah, 2020).

In the GI system, tobacco smoking has been documented to cause harmful effects that contribute to such common disorders as heartburn and peptic ulcers, as seen with COVID-19 and khat (El-Zayadi, 2006; Garland et al, 2020). Consumption of alcohol, on the other hand, produces more serious GI disturbances that could at least lead to diarrhea, gastritis, heartburn and impairment of nutrition absorption (Bishehsari et al., 2017; Bode & Bode, 1997). These overlapping effects of

alcohol with those of khat and tobacco can further worsen the GI effects of COVID-19.

Liver damage

It has been shown that some constituents of khat, including tannins and cathinone, cause liver toxicity with prolonged khat use (Cox & Rampes, 2003; Kennedy et al., 2020; Staurung et al., 2018). This toxic effect can add to the harmful hepatic effects seen with severe COVID-19 (Garland et al., 2020). Further, the consumption of alcoholic beverages by khat users can potentially lead to alcohol-induced liver toxicity (cirrhosis), further raising the risk of liver damage (Dubey et al., 2020; World Health Organization 2020c). The effect of tobacco smoking on the liver, however, is not well defined, although some studies indicate immune and oncogene-related mechanisms (El-Zayadi, 2006). Therefore, the role of tobacco in liver disease as related to COVID-19 awaits further investigation.

Blood clotting

Studies have revealed that tannins in khat and, to some extent serotonin and epinephrine released by cathinone, promote the acceleration of blood clotting and thrombus formation (Abebe, 2018; Al-Alimi et al., 2017; Alkadi et al., 2008). Chronic use of alcohol (as opposed to mild and short-term use), and tobacco smoking have also been reported to cause blood clotting (Dimmitt et al., 1998; Tapson, 2005). Coagulopathy and blood clotting are also known to be among the major pathologies of severe COVID-19 (Dubey et al., 2020; McIntosh, 2020; Vital Strategies, 2020). Thus, the prolonged use of khat, tobacco and alcohol could be a contributing factor for worsening these complications of COVID-19.

Nutritional deficiency and immune suppression

As noted earlier, due to their combined effects of appetite suppression, hepato-GI disturbances and immune modulation, khat, tobacco and alcohol have the potential to cause nutritional deficiency and immune suppression with chronic use (Abebe, 2013; Alvi et al., 2015; Ketema et al., 2015; Wei & Shah, 2020). This situation again enhances the susceptibility of the users to SARS-CoV-2 infection, which in turn leads to greater risks for COVID-19-related complications.

SUMMARY AND CONCLUSION

Given the current global epidemic of substance abuse, there are concerns that individuals who abuse substances could be at greater risks of being affected by the ongoing COVID-19 pandemic. Khat being one of the commonly abused substances, the consequences of its interactions with COVID-19 are reviewed in this paper, along with review of the effects of tobacco and alcohol, which are very often used along with khat. It is likely that the practice of khat chewing can facilitate increased exposure to SARS-CoV-2 and its transmission among chewers. Khat chewers experiencing the adverse consequences of the herb can be at greater risks of being affected by COVID-19 complications, and these risks include the worsening of respiratory, cardiovascular, CNS, renal, GI, hepatic, hemostasis and immune dysfunctions. Similarly, tobacco smoking and alcohol consumption by khat chewers can further facilitate the spread of SARS-CoV-2 and intensify of most of the disorders noted, adding to the burden of COVID-19-related health challenges. Besides

these major observations, the following aspects should also be given due considerations when dealing with this issue.

1. The severity of the effects of khat and the associated substances discussed may depend on various factors, including the type and amounts of substances used, the duration of use, other possible substances consumed and the condition of the user.
2. In tackling SARS-CoV-2 infection and COVID-19 in khat chewers, emphasis should be placed not only on diagnosis and treatment of the infection but also on environmental intervention to control exposure and transmission of the virus.
3. While the literature reviewed deals with the effects of interactions of the substances with COVID-19 on an individual basis, there is no information regarding the effects of combination interactions. Also, in some instances, the literature is limited in providing more specific interaction information, in addition to reflecting general limitations of scope. Therefore, some portion of the reported information is based on indirect evidence from previously published data on specific areas.

Despite the shortcomings noted, it is prudent for healthcare providers and khat chewers to take into account what is currently known and reported in order to appropriately prevent and/or treat the possible harmful effects that could arise due to interactions between COVID-19, and khat and the associated substances mentioned. The research community should also conduct further studies on this important area in order to generate additional and more specific information for increased understanding of the issue

and to help make better informed decision. This review is partly intended to help researchers contribute to this effort.

CONFLICT OF INTEREST

The author declares no conflict of interest in relation to the present work.

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