

## MINI-REVIEW

# Smokeless Tobacco (Shammah) in Saudi Arabia: A Review of its Pattern of Use, Prevalence, and Potential Role in Oral Cancer

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### Abstract

**Background:** Shammah is a traditional form of chewing tobacco [smokeless tobacco, (ST)] that is commonly used in the Middle East especially in Saudi Arabia (KSA), Yemen and Sudan. The Substance Abuse Research Centre (SARC) at Jazan University noted that no adequate research and information on the prevalence of shammah use in the province of Jazan, and KSA as well, has been provided in the scientific literature. **Materials and Methods:** An intensive systematic review of online databases was performed, including AMED (The Allied and Complementary Medicine Database), Biological Abstracts, Cochrane Collection Plus, Dentistry and Oral Sciences Source, E-Journals Database, EBSCO Discovery Service, MEDLINE, PEMSsoft, PEP Archive, PsycARTICLES, scopus, Sciencedirect and Google Scholar. **Results:** Shammah is a mixture of powdered tobacco, lime, ash, black pepper, oils and flavorings. ST in KSA is placed in the buccal or lower labial vestibule of the mouth. The user (or dipper) spits out insoluble debris. The importation of ST products is prohibited in KSA. Accessible information on legislative action to control the use of ST in KSA appeared in 1990. The actual percentage use may be higher, than reported since shammah is illegal in KSA and there may be some reluctance to admit to its use. **Conclusions:** This review paper is an initial step in a funded research project by SARC to understand the pattern of use of shammah and provide adequate epidemiological data. One goal of this review is to generate further data for public health education.

**Keywords:** Saudi Arabia - smokeless tobacco - shammah - oral cancer

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### Introduction

The tobacco plant is considered to have instigated on the mainland between North and South America over 7000 years ago (Haustein, 2010). There are many diverse botanical classifications for tobacco plants. The genus *Nicotiana* is classified into three main subgenera, *N. rustica* (Figure 1), *N. tabacum* and *N. petunioides*. Smokeless tobacco (ST) products use *N. tabacum*, *N. rustica*, *N. glauca* (Figure 1) or *N. nepalensis* (Winter, 2000; Valdes de la Cruz et al., 2010). These varieties differ in their alkaloid composition and, consequently, toxicity. Therefore, the toxicity of these tobacco species and their health impacts may be reasonably different. American Indians were the foremost to smoke, chew and snuff tobacco. The origins of these practices are lost in ancient times. Chewing tobacco and snuff are presently named smokeless tobacco (ST). The term smokeless tobacco was also used to describe the habitual use of unburned tobacco products in the oral cavity (Hoffmann and Hecht, 1985; Russo et al., 2011).

In the United States in 2008, an estimated 8.7 million U.S. adults (3.5%) used ST (Cokkinides et al., 2009). Although ST use rates are historically low compared

to cigarette smoking, ST use in the U.S. is increasing (Stewart et al., 2009). In India, an estimated 28.1% of male and 12.0% of female use ST (Rani, 2003). Approximately 23% of Swedish men are reported to use snus (Foulds 2003). In Sudan, about 40% of males and 10% of females use toombak (local name of ST) (Idris et al., 1996; Idris et al., 1998). Today, the trade of certain types of ST, such as moist snuff, is also illegal in several countries, e.g., in Saudi Arabia, Japan, Hong Kong, Singapore, Australia and New Zealand (Klus et al., 2009).

The unfavorable health side-effects linked with the use of ST include oral cancer, oral leukoplakia (precancerous), cardiovascular disease, periodontal



**Figure 1. *Nicotiana Rustica* (Left) and *Nicotiana glauca* (Right)**

ailments, and nicotine dependence. The possible role that immune dysfunction, including dysregulation of immune cells and their components, may play in the progression of these unfavorable health effects is only just beginning to emerge. Evidence signifying reproductive outcomes, such as perinatal mortality, preterm birth, and decreased sperm viability, also exist in conjunction with ST use. Cardiovascular health may also be impacted by ST use, resulting in augmented blood pressure and dysfunction of CVS endothelia, both of which may possibly lead to cardiovascular illnesses. Intoxicating carcinogens have been examined in ST products, with levels of tobacco-specific nitrosamines 100-fold greater than legal limits for nitrosamines in foodstuffs (Walsh et al., 2010; Warnakulasuriya et al., 2010; Ebbert et al., 2011; Klesges et al., 2011; Bhattacharyya, 2012; Willis et al., 2012). The use of nicotine replacement therapy (patches or gum), and bupropion have not been revealed to assist people to quit ST. However, one study shows that varenicline can assist people stop. Dentists and hygienists may help their patients to quit, especially when they prove them the damage that ST causes in their mouths. Soci- and/or psychological psychotherapy through telephone dialogue may assist ST users in quitting (Ebbert et al., 2011).

A strong relationship linking the use of ST and the presence of oral mucosal lesions has been reported. ST has been associated with an increased risk for oral cancer in the southern United States (Winn et al., 1981). In a study of 1109 professional baseball players in the United States, 203 (18.3%) had oral mucosal lesions; of these affected subjects, 196 (96.6%) were current users of ST (Warnakulasuriya and Ralhan, 2007; Warnakulasuriya et al., 2010). A few studies conducted in KSA reported similar findings (See next section) (Salem et al., 1984; Hannan et al., 1986; Salem, 1989; Allard et al., 1999; Al-Balawi and Nwoku, 2002; Halboub et al., 2011). Carcinogens have been isolated from ST. Researchers have conducted *in vitro* bioassays to test the genotoxicity of ST. Extracts of ST have been established to be mutagenic (Hecht, 2003; Moggetti et al., 2006). *In vivo* experiments have provoked oral cavity tumors in rats by using ST products. *In vivo* experiments with hamsters have demonstrated that ST did induce tumors in the cheek pouch of this animal model (Brunnemann and Hoffmann, 1992; Boffetta et al., 2008).

The literature review designates that the excellence and findings of available analytic epidemiological studies on the theoretical relationship between the risk of oral cancer and the use of ST are variable. Published results do support the need for well-controlled studies which include: a clear defined measures to diagnose patients of oral cancer and to categorize a subject as the users of oral cancer; a dependable way to obtain information from the study subjects; and a clear method to match cases and controls or the use of statistical methods to regulate some important confounders like age, cigarette smoking, and alcohol drinking adequate (Gross et al., 1995).

Shammah is a preparation of ST, being a mixture of powdered tobacco, carbonate of lime, ash, black pepper, oils and flavoring. Shammah is placed in the mouth as a quid. The sites of shammah in the oral cavity has been reported as being: kept in the buccal cavity; retained

in the vestibule of the mouth; permitted to rest in the gingivobuccal sulcus; placed in the lower labial or buccal vestibules (Allard et al., 1999). The use of ST in the KSA is most frequently observed in Jazan province, although it is not restricted to this province. Shammah is also used in Yemen which borders the KSA at Jazan province. The oral use of unburned tobacco (shammah) in Jazan has been reported to begin as young as 10 to 13 years of age. It is also reported to be used with infants to reduce the pain linked with erupting teeth. The real percentage may be higher, since shammah is illegal in KSA and there may be some unwillingness to disclose to its exercise (Hannan et al., 1986; Salem, 1989; 1992; Allard et al., 1999; Halboub et al., 2011). Substance Abuse Research Centre (SARC) at Jazan University noted that no adequate research and information on the epidemiology of shammah in the province of Jazan was provided in the scientific literature. This review paper is an initial step in a funded research project by SARC to understand the pattern of use of shammah and provide adequate epidemiological data. One goal of this review is to engender further data into public health education.

## Different Types of Smokeless Tobacco

Use of smoke-less tobacco (SLT) is very common in South and South-East Asian countries (Valliani et al., 2012). Shammah is used in KSA and Yemen. ST is used without burning the product, and can be used orally or nasally. Internationally, there are more than twenty eight types of orally used and two types of nasally inhaled ST (Kuper et al., 2002; Rodu and Jansson, 2004). Oral ST products are positioned in the mouth, cheek, or lip, and are sucked (dipped) or chewed. Chewing tobacco can be classified as loose leaf (made from cigar leaf tobacco that is air-cured, sweetened, and loosely packed), plug (made from heavier grades of tobacco leaves harvested from the top of the plant, immersed in a mixture of licorice and sugar and pressed into a plug), or twist (air-cured or fire-cured burley tobacco leaves, flavoured and twisted in form of a rope) (Hoffmann and Hecht, 1985). Snuff is a universal word for finely cut or powdered, flavoured tobacco, which can be prepared as moist snuff (air-cured and fire-cured tobacco, flavoured and powdered into fine particles, containing 20-55% moisture by weight) and dry snuff (fire-cured, fermented tobacco powder that may contain aroma and flavour additives) (Brunnemann and Hoffmann, 1992; Boffetta et al., 2008). Tobacco pastes or powders are also used orally and applied to the gums or teeth. Dry snuff can also be inhaled through the nasal passages (Boffetta et al., 2008). In the United States, the major types of ST are chewing tobacco (cut tobacco leaves) and snuff (moist ground tobacco). Table 1 shows an example of five types of ST in the five different countries. In Sweden, 'snus' (finely ground moist tobacco) is used. In India, ST contains tobacco leaf mixed with other ingredients, such as areca nut and lime (Cokkinides et al., 2009; Ebbert et al., 2011). Data from the Global Adult Tobacco Survey-India Report showed that, Khaini, a smokeless tobacco product, is the most popular form of tobacco use among males and females

**Table 1. Different Types of ST. Differences were Stated Based on the Country of Uses**

Country	Local name(s)	Method of use	Method of preparation	References
Sudan	v	Toombak is rolled into a ball that weighs about 10 g and is called a saffa. The saffa is held between the gum and the lip or cheek, or under the tongue on the floor of the mouth.	Toombak is of the species <i>Nicotiana rustica</i> , and the fermented ground powder is mixed with an aqueous solution of sodium bicarbonate. The resultant product is moist, with a strong aroma	(Idris et al., 1998)
Saudi Arabia	Shammah	Placed in the mouth as a quid	mixture of powdered tobacco, carbonate of lime, ash, black pepper, oils and flavoring	(Allard et al., 1999)
Sweden	Snuff, (locally known also as snus)	Snus is manufactured into a dry form used in the nasal cavity and a moist form used in the oral cavity	Finely ground (powdered) tobacco that is sold moist, dry, or in tea bag-like pouches called sachets.	(Idris et al., 1998)
Turkey	Maras powder	Applied to the mucosa of the lower lip for 4-5 min and then it is spit out.	The leaves of the plant ( <i>Nicotiana rustica</i> ) are powdered and this powder is mixed with the ash	(Özkul et al., 1997)

(Bhawna 2013). A study done in Pakistan to evaluate the percentage of hospital staff that use ST, and to categorize the factors connected with its use and their practices. The study showed that a high percentage of paramedical staff of public sector hospitals consume ST in different forms. Most common type consumed is 'Gutka' and their family or friends influenced approximately half of them (Valliani et al., 2012). A relatively high prevalence of smokeless tobacco consumption among the male students of universities of Zahedan, Iran (Honarmand et al., 2013).

### Oral Cancer and Shammah in Saudi Arabia

Elongated period chewing of tobacco or the use of snuff has been associated with cancer of oral cavity, cheek, gums and oropharynx (Albar, 1994; Willis et al., 2012; Foulkes, 2013). Oral cancer is one of the ten most frequent cancers in the world (Jemal et al., 2010; Jemal et al., 2011). Approximately two thirds of the worldwide occurrence of oral cancer happens in the Indian subcontinent, as a result of the widespread tobacco chewing custom in the population. Regardless of advancement in treatment modalities, the five-year survival rates have remained unchanged over the past 20 years (Mallick et al., 2010). In Bangladesh, India, Pakistan and Sri Lanka, it is the most common malignant ailment and it accounts for a third of all malignancies (Ferlay et al., 2010; Moore et al., 2010; Johnson et al., 2011; Khan, 2012; Raveendran and Nath, 2012). More than 100,000 new cases occur yearly in South and South East Asia. The commonest cause for oral cancer is tobacco chewing, usually in the form of betel quid which consists of betel vine leaf (pipe betel), areca nut, lime and tobacco (Priebe, 2009; Jalouli, 2010).

The substantiation that ST causes oral cancer was established recently by the International Agency for Research on Cancer (Petersen, 2009). Only a few reports on ST chewers and associated oral lesions were published (Zhang et al., 2001). Hannan et al. described a brand of ST and its potential carcinogenicity on the basis of in vitro bioassays (Hannan et al., 1986). Hannan et al. (1986) showed the mutagenic potential of shammah by use of the *Salmonella typhimurium*/microsome mutagenicity assay (Ames test), aberrant colony formation and mitogenic gene conversion in yeast, tryptophan gene conversion in the D7

diploid strain of *Saccharomyces cerevisiae* and in vitro oncogenic transformation in C3H mouse embryo 10T1/2 cells. Another study by Samman et al. showed that mint may prevent Shammah-induced carcinogenesis in hamster cheek pouch (Samman et al., 1998). Effects of ST on oral keratinocytes observed in vitro include alterations in cell proliferation, apoptosis and activation of inflammatory markers. Genetic aberrations caused by ST include activation of ras, uncommon in smokers but mutational hot spots in p53 encountered are similar to those in smokers (Warnakulasuriya and Ralhan, 2007). Previous studies have demonstrated that an aqueous ST extract when given in a single oral dose to experimental rats results in an superior induction of liver lipid peroxidation, hepatic DNA single strand breaks (apoptosis marker), and a marked augmentation in the urinary excretion of the lipid metabolites malondialdehyde, formaldehyde, acetaldehyde, and acetone (Bagchi et al., 1994; Bagchi, 1997; Chole et al., 2010; Ramya et al., 2011; Kurtul and Gökpınar, 2012). A previous study indicated that the acute exposure of HOK-16B cells to ST leads to cell death, at least in part, through oxidative stress via up-regulation of ASK1 and the JNK 1/2 and p38 signaling pathways. These findings provide an established scientific explanation to the ulceration and inflammation observed in people using ST at a new site within 2 days (Mitchell et al., 2010).

Oral cancer is the 3rd most frequent reason of malignancy in KSA after lymphoma and leukemia (Tandon et al., 1995; Jaber et al., 2011). Malignant oral cavity tumors represent approximately 26% of all head and neck cancers detected yearly in KSA. The majority of cases are advanced, and palliatively treated. The high incidence of oral cancer in KSA is attributed to frequent use of tobacco (Shammah). Several authors have reported their clinical impression that the high frequency of oral cancer in the southwestern region of the KSA, and predominantly in Jazan province, was related to the use of shammah. In one report, 89% of the patients with oral cancer provided a history of shammah habit. In another study, 49% of the patients with oral cancer confessed to using shammah (Salem et al., 1984; Salem, 1989, 1992; Allard et al., 1999; Halboub et al., 2011). An epidemiological appraisal of oral cancer among 26, 510 Saudi cancer patients from all regions of the KSA over 20

years recognized one region-Jazan, as the source of 35.4% of those oral cancer sites in the proximity of the habitual intraoral placement of shammah. These data suggest there is an association between shammah, oral cancer, and Jazan region: oral cancer appears to be more common in this region where shammah is also common (Allard et al., 1999). A study was conducted on Oral Maxillofacial Surgery Unit of the Armed Forces Hospital, Riyadh, KSA to analyze the manner of cure and subsequent outcome of 228 oral cancer patients. The study showed that oral cavity tumors are the most common neoplasms in the Jazan region of KSA. They represent 13% of all cancers and 72% of head and neck cancers diagnosed annually in this area. Authors claimed that this high incidence of oral cancer is attributed to "shammah" using habit (Al-Balawi and Nwoku, 2002).

While carcinogenicity of ST to humans is well established the oral lesions that precede development of cancer are less well characterized. The clinical appearances of ST-associated lesions are variable (Warnakulasuriya and Ralhan, 2007). The most frequently reported sites of oral cancer among shammah users in one report were tongue (33%) and oral vestibule (32%) (2); in another study, tongue (15%), floor of mouth (18%), retromolar trigone (18%), and buccal mucosa (49%). Morphological features observed are somewhat different to oral lesions caused by smoking and oral dysplasia in shammah-associated lesions is less common (Warnakulasuriya and Ralhan, 2007). A study included Saudi citizens from the general population, in an age range from 20 to 57, composed of males and females. Of the 1436 subjects studied, 226 (15.7%) had clinically diagnosed lesions of the oral cavity mucosa. Among the affected subjects with these lesions, 98.7% approved the use of shammah. The location of oral mucosal lesions among shammah users included: tongue, floor of mouth, lower lip, labial vestibule, cheek, buccal vestibule, alveolar mucosa and gingival mucosa (Tandon et al., 1995; Allard et al., 1999).

Oral squamous cell carcinoma (OSCC) is a remarkably common malignancy of the mouth, with high morbidity (Gerva'sio et al., 2001; Kuffer and Lombardi, 2002; Llewellyn et al., 2004). Although OSCC has a relatively good prognosis, patients who do not receive early treatment have a low 5-year survival rate (Matsumoto et al., 1999; Miller et al., 2003). Among premalignant lesions, leukoplakia (LKP) is a potentially malignant lesion of the oral mucosa when it shows histological features of epithelial dysplasia, while oral LKP without dysplasia has a lower risk of malignant transformation (Van der Waal and Axell, 2002). Oral LKP had been reported as the most premalignant lesion of the mouth in the Southeast Asia subregion. The rate of malignant transformation in oral leukoplakia varied from 6% in some studies to even higher figures in others (Axell et al., 1996; Neville and Day, 2002). A study done by Salem (1992) on the prevalence of leukoplakia in relation to tobacco habits (n=1,436) at Jazan Region, KSA. The prevalence rate of oral leukoplakia and preleukoplakia in this study were 11.4% and 4.3%, respectively. Of the affected subjects, 99% were dippers of snuff known as Shammah. Authors observed that the location of the oral lesion was almost

always consistent with the site where the snuff was habitually held. A smaller proportion of lesion was found in Shisha smokers while none of those who only smoked cigarettes had leukoplakia or preleukoplakia. Findings of this research provided evidence that a relationship exists between oral leukoplakia and Shammah dipping (Salem, 1992). In another study by Salem and his research group in King Fahd Central Hospital, Departments of Dentistry and Histopathology, Jazan, Saudi, Arabia, a survey of the oral mucosa in 661 of the people living in Jazan region has been carried out. Oral leukoplakia have been found to affect approximately 68% of the users of the native snuff known as Shammah. The results of that study point to a possible causal relationship between the use of 'Shammah' and the development of oral premalignant and malignant lesions among snuff-dippers in the Jazan region (Salem et al., 1984). Epidemiological studies show a strong significant association of risk with chronic daily use but population differences are noted because of various commercial products in use (Warnakulasuriya and Ralhan, 2007). As Jazan is socially and geographically associated with Yemen. As study done in Yemen gave evidence for a significant association of the prevalence of oral leukoplakia with the daily duration of the contact of shammah with the oral mucosa in a dose-dependent manner. In addition, a lack of knowledge on shammah disadvantages and a lack of ability to quit this habit were inversely associated with oral leukoplakia. Clinically, the latter should give reason for an intensive public health care information campaign on the carcinogenicity of shammah, as oral carcinomas were found with a prevalence of 1% in this sample of shammah users (Scheifele et al., 2007).

Sawair et al., (2007) studied the association of khat chewing and tobacco consumption with the occurrence of oral cancer in Sana'a, Yemen. A total of 649 cases of primary malignant tumors (348, 53.6% males and 301, 46.4% females) were extracted. Oral cancer was the most frequent body cancer in both males (17.2%) and females (19.6%). Squamous cell carcinoma (SCC) was the most frequent oral cancer (84%), and the tongue (42%), gingiva (23%) and buccal mucosa (20%) were the most common sites. Simultaneous chewing of tobacco and khat was found in 48 cases (52.2%). That survey has disclosed that oral SCC is the most frequent cancer in Yemen, and that the high relative frequency of oral SCC may be related to the habits of chewing tobacco and khat (Sawair et al., 2007). Yemenis immigrants are also working KSA. In study by Halboub et al., (2011), the characterization of Yemeni patients treated for oral and pharyngeal cancers in KSA were investigated. There were 5862 Yemenis registered with malignancies. Oral cancer ranked the eighth most common malignancy (215, 3.7%) with 1.65:1 male to female ratio. The squamous cell carcinoma was the most frequent morphological type (289, 63.5%) but significantly more frequent in oral cancer. Approximately, 56% (255 patients) were diagnosed at advanced stage, however, significantly more frequent in PC (155, 64.6%) (Halboub et al., 2011). Authors in that retrospective study (1994-2007) and in light of their findings, assumed the etiological role of the indigenous habits of khat chewing and shammah as causative agents of oral cancer (Halboub

et al., 2011).

Recently, Al-Attas and his research group recruited about 600 tobacco users. Samples of such study underwent clinical conventional oral examination and filled a questionnaire providing information on demographics, tobacco use and other relevant habits. The most common form of tobacco used was cigarette smoking followed by Shisha, ST, betel nuts and Khat, respectively (Al-Attas et al., 2014). They concluded that ST was associated with a wide range of oral mucosal lesions (Al-Attas et al., 2014).

Toombak, a chewing tobacco from Sudan, causes similar changes as the ones described for Shammah. Both clinical and histological changes of Toombak-associated oral mucosal changes and those observed for Shammah are comparable. Idris et al. found parakeratosis, pale surface staining of epithelium and basal cell hyperplasia in their material. Epithelial dysplasia was infrequent. The Toombak-associated leukoplakia was compared to the Swedish moist snuff dipper's lesion (Abbas and Ahmed, 2013; Ahmed and Mahgoob, 2007; Idris et al., 1996).

### Some Recommendations of Previous Work on ST Quitting

As mentioned earlier SARC noted that no adequate research and information on the prevalence of shammah use in KSA was provided in the scientific literature. This review paper is an initial step in a funded research project by SARC to understand the pattern of use of shammah and provide adequate epidemiological data. One goal of this review is to generate further data into public health education. As SARC also is attempting to adopt some of the previous health promotion and education strategies, author is briefing some of the previous international efforts in these aspects. Previous studies suggested the importance of conducting research to identify factors associated with successful tobacco quit attempts may help in the development and targeting of effective cessation strategies (Christen, 2001; Zhu et al., 2002; Kauffman et al., 2008). Further research is needed to study ST addiction with the assistance of a theory driven complete scale that has superior psychometric properties (Spielberger et al., 1995; Haddock et al., 1999; Ebbert et al., 2011). With the rising marketing of alternate tobacco products, support of harm-reduction, and smoke free air policies, an overall increase in ST use has been observed since the 1970s. Many studies have been published addressing nicotine dependence measures for smokers; however, research in the field of ST dependence measures is scarce (Heatheron et al., 1991; Mushtaq and Beebe, 2012). Some Research is also needed to examine the effects of brand switching on levels of nicotine intake and toxicant exposure among ST users (Hatsukami et al., 2007). As KSA is Islamic country, special issues should be considered. Islamic teachings forbid smoking. There are hundreds of Fatwas (decrees) that ban ST and smoking since its first beginning in Islamic countries. If the Muslims stick to these Fatwas, they will eliminate a major cause for cancer. It will also decrease the deaths due to other lung diseases and ischemic cardiac diseases which showed persistent increase in most Islamic

countries (Albar, 1994).

Studies to de-assemble behavioural interventions to recognize successful core components such as telephone counselling or oral examinations with feedback (Ebbert et al., 2007) are highly recommended to be applied in KSA social setting. These also include comparisons of various nicotine replacement therapy (NRT) doses, forms, and durations of therapy and combination therapies using both non-nicotine pharmacotherapy and NRT.

### Conclusions

This review paper is an initial step in a funded research project by SARC to understand the pattern of use of shammah and provide adequate epidemiological data. One goal of this review is to generate further data into public health education.

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