Oral lesions in patients consuming different types of smokeless tobacco. A literature review.

Lesiones orales en pacientes consumidores de diferentes tipos de tabaco no inhalados. Revisión de la literatura.

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Abstract

Introduction:

Smokeless tobacco (ST) is widely consumed around the world, with products such as gutkha and paan masala being particularly common. These products typically contain areca nut, which is known for its carcinogenic properties and negative effects on oral health. In addition, tobacco is a key ingredient in ST and has been linked to a range of general and dental health issues, particularly among younger populations. Aim: The purpose of this article is to review the literature about ST and its repercussion on the oral health, specifically the dental and periodontal effects.

Method:

This research was based on a systematic review of articles published between January 2009 and March 2023, aided by PubMed, Scielo, and Google Scholar search engines. Conclusions: Some studies have shown that ST and areca nut components can be particularly dangerous for people with cardiovascular disease and diabetes. Additionally, tobacco has a significant impact on periodontal and dental health, with pathological lesions that may lead to malignant disorders. Peer pressure and stress are common reasons for ST addiction. As such, promoting the intention to quit this habit should be repeatedly emphasized to avoid the negative consequences of these products.

Key Words:

smokeless tobacco, gutkha, areca nut, diabetes, cardiovascular disease, periodontal disease, dental caries, intraoral lesions.

Introduction

The worldwide tobacco outbreak has caused a wide range of health effects and is the main cause of oral cancer. It's been considered the most consequential threat to human health globally. Over the time, the use of various types of tobacco has escalated in Asia, primarily in India.

Additionally, it has been observed in Asian immigrant communities in Europe, North and Central America. (Pandey et al. 2019).

Tobacco use has prompted around 800,000 deaths annually, for which the majority were led by smokeless tobacco (ST) products such as betel, snuff, gutkha (paan masala), and mishri. (Agrawal et al. 2020) These products are an important factor in the causes of addiction and death in the Indian population. ST persists as the most pervasive form of tobacco usage after cigar, cigarettes, and electronic cigarette. (Willis et al. 2014).

Its use has shown an immense surge in the young population worldwide and adolescents

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and young individuals are inclined to these habits quickly by the influence of friends and relatives. Furthermore, this group has the tendency of trying the products for fun without having any knowledge of the consequences and effects of the diverse products containing tobacco. (A'yun et al. 2022).

One of the most common forms of ST use is the gutkha (or betel quid), Its main ingredient is the areca nut (seed of the areca palm), it also contains crushed tobacco, slaked lime (calcium hydroxide paste) and catechu (extract from the acacia plant). This is also blended with sweeteners and flavoring agents. Gutkha is placed between the cheek and gum and can be chewed or sucked. The consumer may spit the saliva out or swallowed the product. (Harini et al. 2022).

This product has made a substantial headway within a lower socioeconomic status population as an alternative for smoking. Consumption has increased throughout the years, possibly, because of the great amount of publicity placement under many brands, and as a result of the reasonable cost in local markets. (Shukla et al. 2020).

On the other hand, the strategic plan of selling gutkha in small shops and kiosks near malls and schools, has enabled the accessibility and effortless spread of this addiction in young individuals and children in India. (Srivastava. 2014).

Furthermore, gutkha provides the same effects of cigarettes as it also contains nicotine, so it may be used as a replacement for them. It has been clearly demonstrated that the use of cigarettes, gutkha or any other product containing tobacco, is difficult to quit, and consequently, is creating an addiction among its users. (Banerjee et al. 2013).

The essential element of gutkha, areca nut is the seed of the areca fruit from the tropical palm areca tree which is found greatly in parts of South Asia. (Gupta et al. 2015). The main ingredient of gutkha is known to be a human carcinogen. It contains several constituents, such as tannins, that act as stimulants and alkaloids, especially arecoline. Areca nut is consumed by roughly 600 million people globally, most of them belong to low socioeconomic status. In the same manner as gutkha, areca nut is placed between the gum and cheek (Do et al. 2022).

Another option is snuff, which is known as a type of ST made of finely ground or shredded tobacco leaves. It can have various types of flavors and scents and it is also positioned between the gum and cheek or behind the upper or lower lip. It has been related to heart illness, gum disease and other health problems. (Harini et al. 2022).

Tobacco-specific nitrosamines, which appear during the curing and processing of tobacco, are available in all commercial tobacco products, including smokeless tobacco, cigarette smoke, and cigar smoke.

There are seven tobacco-specific nitrosamines found in unburned, cured tobacco, but only three of them have received attention: N'-nitrosonornicotine (NNN), 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanone (NNK), and its main metabolite 4 -(methylnitrosamino)-1-(3-pyridyl)-1-butanol (NNAL). There is evidence for their endogenous synthesis, mainly via the nitrosation of nornicotine. Cured and processed tobacco

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are the essential sources of tobacco-specific nitrosamines, which are fabricated when tobacco alkaloids react with nitrite. Two tobacco-specific nitrosamines NNN and NNK, with mean concentrations of 1901 ng/g and 523 ng/g, respectively, are the most carcinogenic (Sankla et al. 2017).

NNN and nicotine are both found in ST products. It must be pointed out that NNN is expected to have a significant role as a cause of cancer, and an important fact to understand is that the nitrosation of nicotine may lead to the formation of NNN. (Hecht et al. 2022).

The purpose of this article is to review the literature about ST and its repercussion on the oral health, specifically the level of effect on the dental and periodontal side.

Methodology

A bibliographic search was conducted on PubMed, Google Scholar and Scielo, for articles published between January 2009 to March 2023 on the effects of the consumption of paan and gutkha on oral cavity. The use of smokeless tobacco in association with topics such as:

- Gutkha,
- Areca nut,
- Ingredients,
- Placement site,
- Association with oral cancer,
- Periodontal status,
- Oral lesion on the oral cavity,
- Effects on the mucosa,
- Periodontal and bone level,
- Dental caries

were added to the inclusion criteria in this investigation. Key words relating to conventional cigarettes, electronic cigarettes, articles not completed, and articles published before 2009 were excluded.

Results

A considerable amount of people consume various types of smokeless tobacco products worldwide, most often gutkha and betel quid. These users are very susceptible to developing oral and general health problems. ST combines several components, the most important being areca nut, which is known to produce carcinogenic and toxic chemicals in the body. The most serious health repercussion of ST is oral cancer. Moreover, different effects will be mentioned and explained regarding general health, intraoral lesions, dental and periodontal status. (Shukla et al. 2020).

Systemic Diseases

It is well established that the usage of tobacco increases the risk of developing cardiovascular disease. It may cause effects such as: increment of myocardial workload, coronary vasoconstriction, reduction of the oxygen-carrying capacity of the blood and induction of hypercoagulable state. ST products contain nicotine, hydrocarbons, nitrosamines, aldehydes, alkaloids, and metal.

ST usage can produce more durable and sustained levels of nicotine, unlike cigarette smoking, which delivers peaks in nicotine level. In the other hand, acute cardiovascular effects

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are common with ST products. These include an increase in heart rate and blood pressure levels. (Shaik et al. 2020) Over the past two decades, substantial evidence has been gathered concerning the possible association between tobacco and the development of systemic diseases such as diabetes. Health risks due to smoking have been reported to be higher for people diagnosed with diabetes than for the general population. Studies have stated the effect of ST usage over diabetes, glucose levels, glucose intolerance, insulin levels and insulin intolerance.

Intraoral Lesions

Tobacco use is increasing rapidly. It is most popular with young adults as an alternative to smoking. ST products contain various carcinogen chemicals which are associated with different types of oral cancer.

As ST is placed intraorally, it can induce to changes in the oral cavity resulting in pathological lesions. (Jyoti et al. 2012) The oral effects of ST are seen primarily where the product has been placed. If these intraoral lesions are not managed at an early stage, it is most likely to develop oral cancer. The presence of dysplastic changes cannot be predicted, and a biopsy must be done on the suspected site. (Le et al. 2022)

The term precancer can be attributed to benign mucosal alterations that can lead to malignant lesions. Prime prevention of general and oral diseases consists of recognition and correct diagnosis of potential malignancies. (Asthana et al. 2019) The World Health Organization (WHO) differentiated between conditions and precancerous lesions. The team outlined a precancerous lesion as an altered tissue in which cancer is more likely to develop. Such lesions are considered potential malignant disorders, for example: leukoplakia, erythroplakia, oral submucous fibrosis and lichen planus. (Warnakulasuriya et al. 2022).

Leukoplakia was defined by the WHO as a white patch or plaque that cannot be characterized clinically or pathologically as other diseases.

The pivotal microscopic feature is the presence of epithelial dysplasia. This lesion can be divided under two types of diagnosis: homogenous and non-homogenous. Homogenous leukoplakia lesions are uniformly flat and thin and can display shallow cracks in the surface keratin.

Non-homogenous leukoplakia present mixed white and red areas although it holds a dominant white character. They are associated with a specific oral site. People who consume gutkha are affected more often on the buccal mucosa where the gutkha is placed. Detection and management of this lesion can prevent the progression of oral cancer.

Although, the presence of epithelial dysplasia is a feasible indicator of malignant potential. Lesions with epithelial dysplasia are 10 times more prone to malignant transformation. (Souza et al. 2009)

Erythroplakia is defined as any lesion of the oral mucosa that displays as bright red velvety plaques that cannot be characterized clinically or pathologically as any other definable condition. Even though it is not as common as leukoplakia, it is much more likely to develop into dysplasia or carcinoma.

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A biopsy is mandatory in all cases of erythroplakia. The favorable way to manage this lesion would be surgery and regular follow-ups complemented by habit reduction. Erythroplakia should be treated soon after diagnosis. (Athukorala et al. 2021)

Oral submucous fibrosis (OSF) is a chronic disorder that develops by fibrosis of the lining mucosa of the upper digestive tract involving the oral cavity, and oropharynx. The oral mucosa hardens because of the fibrosis of the lamina propria leading to a reduction of the mouth's opening range.

OSF is related to the consumption of areca nuts, particularly in chewers of this product. Consuming it may lead to oral cancer. (Singh et al. 2011) OSF occurs across all the intraoral cavity, and it can even extend to the pharynx and esophagus.

Clinically, marked mucosal blanching is observed, prominently in the early stages. Additionally, a diagnostic feature is the presence of palpable fibrous bands in the buccal mucosa and in the lips. Patients might feel a burning sensation and hyper- or diminished salivation and speech defects. OSF is known to be difficult to manage.

Several treatments have been suggested, such as surgical options, although there is no confirmed treatment to restore the normal texture of the oral mucosa and reduce the risk of cancer development. (Athukorala et al. 2021)

Lichen planus is mainly a dermatological disorder in which various mucosal surfaces may be involved. The oral mucosa is more frequently affected than other mucosal sites. It is known to be probably related to immune system malfunctioning. Tobacco use seems to play a role in its development. This oral lesion has shown a great association with gutkha, paan masala and ST products as well. However, tobacco use is not regarded as an etiological factor for this lesion.

Oral lichen planus is diagnosed when a pale, reticular or lace like pattern of striae on the oral mucosa or tongue is observed. Other clinical forms of this disorder are the erosive and ulcerative type. This alteration may lead to oral cancer. (Srivastava. 2014)

Other types of lesions in the oral cavity associated with the use of ST is tooth decay. Dental caries is the most prevalent disease to man, affecting more than 2 billion people worldwide. Tobacco consumption alters the dental composition. It has shown that nicotine increases biofilm formation and bacterial adherence.

Studies show that chewing tobacco and smoking can promote significant health risk factors for dental caries. Reports have acknowledged that ST users have a higher caries incidence. This could be a consequence of the degenerative effect of tobacco on salivary glands.

It can also inhibit the buffering capacity of saliva, making the person vulnerable to cavities. In addition, ST products containing areca nut have also been observed to produce tooth wear, dental sensitivity, and halitosis. Figure 1 shows the effects of each ingredient of ST. (Bhavsar et al. 2022).

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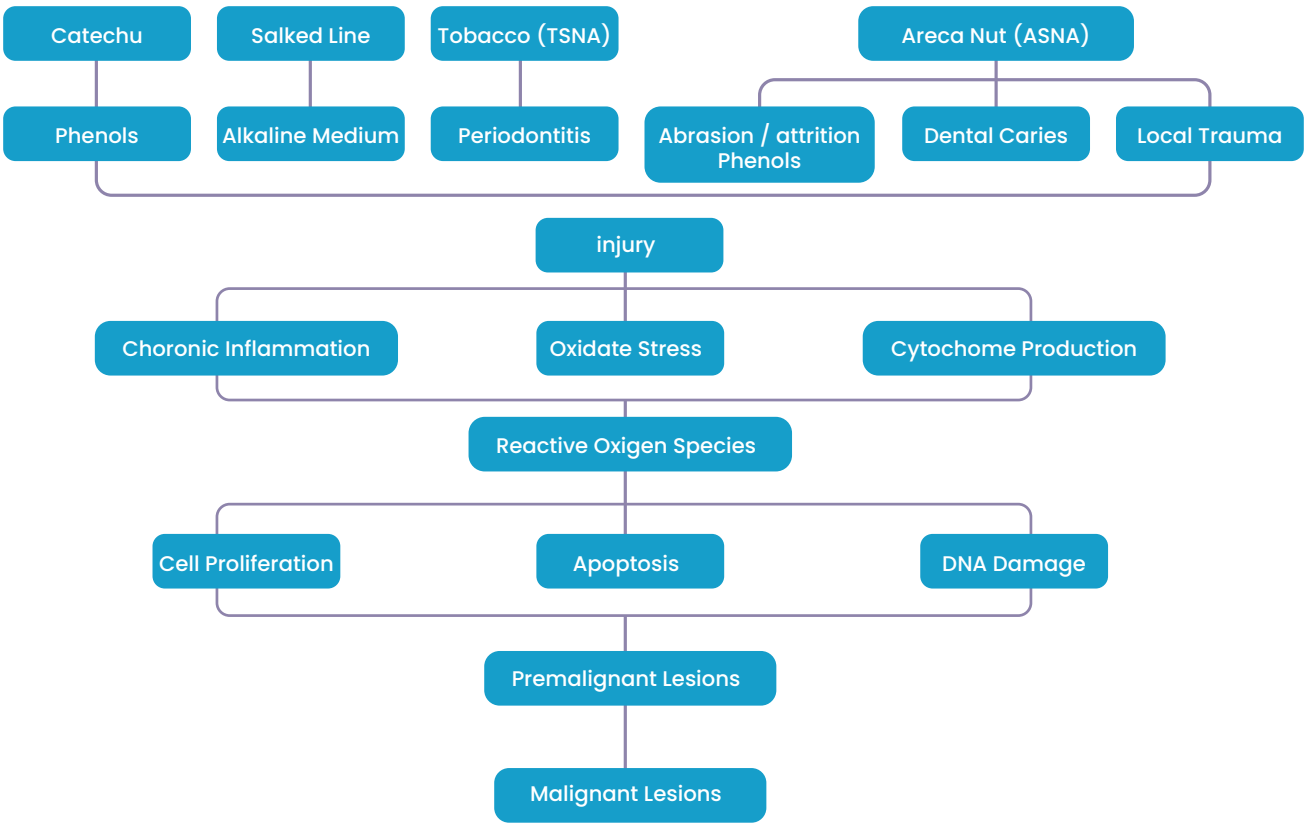

Figure 1. Mechanism of gutkha carcinogenicity. (Sankla et al. 2017)

Reports have revealed a relationship between tobacco and periodontal disease. The consumption of gutkha has been linked with periodontitis and bone decay. (Verma et al. 2019) Periodontal disease is an inflammatory illness of the supporting tissue of the teeth caused by microorganisms and resulting in the progressive destruction of periodontal ligament and alveolar bone. (Dave et al. 2023) Smokers have a higher susceptibility to periodontitis and are less prone to gingivitis.

Possibly because smoking interferes with the inflammatory and immune responses. Smokers are almost 6 times more likely to develop periodontal destruction. (Shah et al. 2021)

The impact of ST products is quite high on all periodontal health indicators such as calculus, plaque and gingival index, gingival recession, clinical attachment loss, furcation, mobility, pocket depth, and formation of lesions. (Mishra et al. 2013) The hardness of the areca nut and the interaction among the various components of chewing products with periodontal tissues might be the reason of poor periodontal health in gutkha chewers. (Hsiao et al. 2015)

Areca nut contains alkaloids (arecoline), and this may play a significant role in periodontal disease in combination with oral hygiene, general health, and dental status. (Kulkarni et al. 2016) The diverse changes in health and oral cavity for gutkha users are listed on Table 1.

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Table 1.
Effect of gutkha on health. (Sankla et al. 2017)

Clinical Changes		Functional Changes
Extra Oral	**Intra Oral**	
Sunken cheek	Whitening of the oral mucosa	Varying degree of trismus
Stiff cheek	Reduced and stiff oral aperture	Speech
Pseudo-proptosis	Bald tongue	Swallowing
Multiple perioral skin folds	Discoloration of the commissure	Reduced salivary outflow
Pseudo malar prominence	Retracted erythematous soft palate and uvula	Dysphagia
	Forward pointing uvula	Hearing
	Loss of tonsillar bulge	Poor oral hygiene
	Oral melanosis	
	Chronic non healing ulcers	
	Oral submucosa fibrosis	
	Calculus	
	Discoloration of tooth	
	Dental caries	
	Attrition/Erosion	
	Extreme sensitivity in teeth	
	Gingivitis	
	Periodontitis	
	Loss of gingival sulcus	

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Table 2. Shows some of the literature that has been published in the last decade addressing the effects related to gutkha and areca nut with its repercussions in the oral health in chewers.

Table 2.
Studies reporting effects of tobacco chewers

Reference	Country or Region	Study Design	Exposure	Effects
A'yun et al. 2022	West Nusa Tenggara	Cross-Sectional Survey	Chewers vs non chewers	Significant relationship between betel chewing with periodontal status
Bhavsar et al. 2022	India	Cross-Sectional study	Chewers vs non chewers	Higher prevalence of dental caries in gutkha users
Harini et al. 2022	India	Case Control	Chewers vs non chewers	OSF
Le et al. 2022	New York, USA	Retrospective study	Users' vs nonusers	High risk of oral lesions, bruxism and frequent consumption of sugary beverages and snacks
Warnakulasuriya et al. 2022	Taiwan	Cross-Sectional	Chewers vs non chewers	Oral cancer with betel quid chewing
Ahad et al. 2021	Asia	Cross-Sectional Survey	Users' vs nonusers	Users have poor oral hygiene and severe gingivitis
Anand et al. 2021	India	Cross-Sectional Survey	Users' vs nonusers	Periodontal destruction significant in ST users
Athukorala et al. 2021	Asia	Literature	Chewers vs non chewers	Areca nut chewers associated with withdrawal symptoms, peer pressure and behavior
Dave et al. 2021	India	Case Control	Chewers vs non chewers	Periodontal index and attachment loss
Shah et al. 2021	Nepal	Comparative	Chewers vs non chewers	High presence of missing teeth in tobacco chewers
Shaik et al. 2021	India	Experimental	Chewers vs non chewers	Significant increase in plasma glucose levels, total cholesterol and decrease in lipoprotein
Agrawal et al. 2020	India	Cross-Sectional Survey	Chewers vs non chewers	Clinical inflammation if gingiva was greater in placement sites of ST
Do et al. 2020	Georgia, USA	Focus Group	Users' vs nonusers	Addiction and gutkha use have affected children

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Shukhla et al. 2020	Ranchi, India	Cross-Sectional study	Chewers vs non chewers	Significant changes were observed in serum IgA and IgG levels in chewers
Asthana et al. 2019	India	Literature	Users' vs nonusers	High association between oral cancer and ST
Pandey et al. 2019	India	Prospective Survey	Chewers vs non chewers	Cause of oral, esophageal, pancreatic and lung cancer
Verma et al. 2019	Delhi, India	Cross-Sectional Survey	Chewers vs non chewers	ST use related to periodontitis, bone misfortune and tooth misfortune
Niaz et al. 2017	Asia	Bibliographic	Chewers vs non chewers	Periodontal inflammation, increased arterial blood pressure and heart rate
Rizvi et al. 2017	India	Cross-Sectional Survey	Chewers vs non chewers	Elevated destruction in plaque, gingival and calculus index, pocket probing depth, recession, and furcation
Sankla et al. 2017	India	Literature	Chewers vs non chewers	High concentration of nicotine responsible for addiction
Goyal et al. 2016	India	Cross-Sectional Survey	Chewers vs non chewers	Consumed ST due to advertisements and good taste
Kulkarni et al. 2016	India	Cross-Sectional Survey	Chewers vs non chewers	Plaque index higher in ST users
Singh et al. 2016	India	Cross-Sectional Survey	Users' vs nonusers	High percentage of recession and clinical attachment loss in gutkha users
Gutpa et al. 2015	India	Literature	Users' vs nonusers	Oral cancer and leukoplakia
Hsiao et al. 2015	Taiwan	Cross-Sectional Survey	Chewers vs non chewers	Plaque and gingival index, bleed on probing, probing depth, clinical attachment loss
Kumar et al. 2014	India	Case Control	Chewers vs non chewers	Leukoplakia, erythroplakia, reverse smoking, lichen planus and OSF
Smita et al. 2014	New York, USA	Focus Group	Users' vs nonusers	Social and cultural influences on tobacco related health disparities
Warad et al. 2014	India	Cross-Sectional Survey	Chewers vs non chewers	High relation with pocket probing depth, gingival index, and clinical attachment loss

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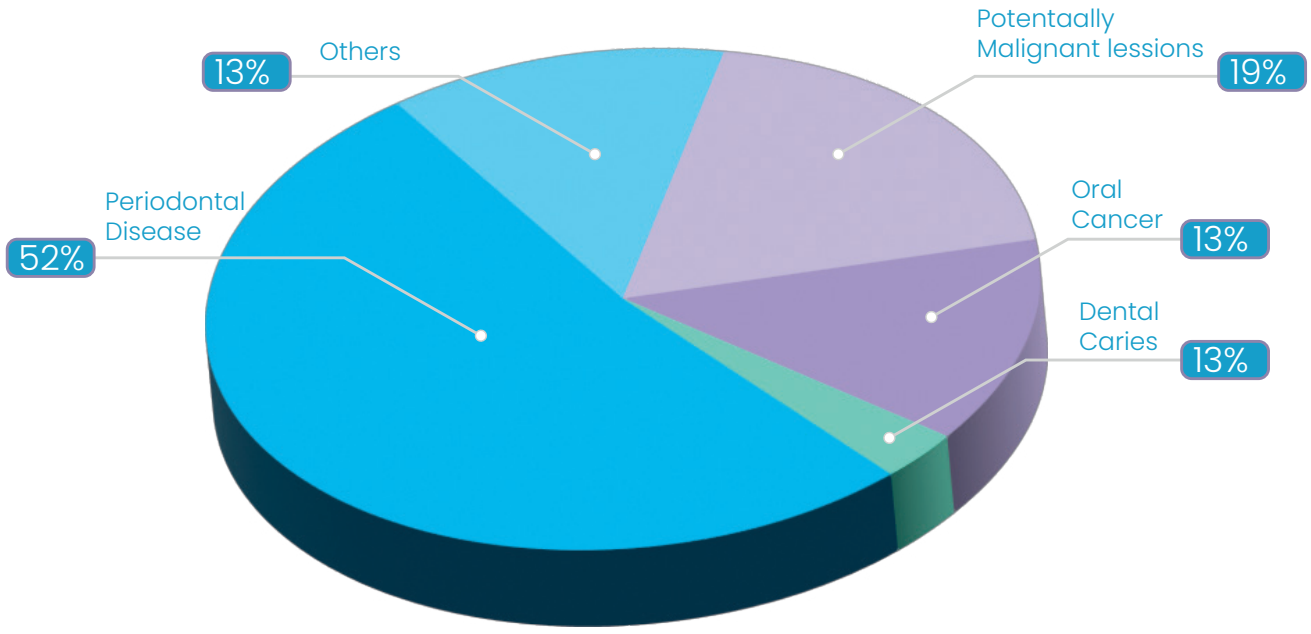
Willis et al. 2014	USA	Experimental	Chewers vs non chewers	Organ system toxicity, critical circulating hormone and enzyme levels
Mallikarjuna et al. 2013	India	Case Control	Users' vs nonusers	Staining of teeth, irritation, burning sensation and bad breath
Mishra et al. 2013	India	Literature	Chewers vs non chewers	ST is considered as a significant risk factor in implant patients
Jyoti et al. 2012	India	Case Control	Chewers vs non chewers	Micronucleus frequency incremented in chewers
Singh et al. 2011	India	Cross-Sectional Survey	Chewers vs non chewers	Great association with plaque, gingival and calculus index, recession, mobility, furcation, and lesions
Auluck et al. 2009	Canada	Literature	Chewers vs non chewers	Oral cancer, oral precancerous lesions
Souza et al. 2009	India	Comparative	Chewers vs non chewers	Lesion such as OSF, leukoplakia, erythroplakia, nicotine stomatitis, palatal lesions, actinic keratosis, and tobacco pouch keratosis

Graph 1. Effects of gutkha in the health



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In Graph 1, a distribution can be observed relating to the effects of gutkha and paan with its consequences in the oral cavity reported by the 31 articles referred to by Table 2. It was found to have a high relation with periodontal disease like gingivitis, periodontitis, bleeding on probing, gingival recession, clinical attachment loss, furcal lesions, increase in biofilm index, calculus index, and pocket probing depth. Periodontal disease was a predominant problem among chewers of gutkha and was mentioned in 51.61% of the articles. In Graph 1, the slice referring to others includes effects such as: bruxism, bad breath, staining in teeth, esophageal, pancreatic and lung cancer, increased arterial blood pressure and heart rate.

Potentially malignant oral lesion among chewers showed a 19.36%, and included: OSF, leukoplakia, erythroplakia, nicotine stomatitis, palatal lesions, actinic keratosis, tobacco pouch keratosis, reverse smoking, and lichen planus.

Discussion

Gutkha is the most consumed presentation of ST, especially in countries like India. It contains many carcinogens, among them is nicotine which is presumed to be the cause of addiction to this product. Other carcinogens found in gutkha are areca nut, catechu, and tobacco. (Auluck et al. 2009) Tobacco affects the general health, as it can increase arterial blood flow and heart rate. The consumption of ST has proven to cause intraoral lesions that can develop to oral cancer.

These injuries cause dysplastic changes in the mucosa which result in alterations in periodontal and dental status. (Niaz et al. 2017)

It is noteworthy that several studies have reported that areca nut components generate reactive oxygen species (ROS) in the oral cavity of chewers. However, saliva has the potential to inhibit the production of these ROS and other free radicals from the constituents of the betel quid. Moreover, paan and gutkha consumption can expose users to various oral mucosal disorders.

Impaired glycemic status has been associated with an increased production and accumulation of ROS in body tissues, including the periodontium. Thangjam and Kondaiah 2009, demonstrated, in an experimental study, that the oxidative stress induced by arecoline alters the inflammatory processes in human keratinocytes. Additionally, paan and gutkha chewers have been found to exhibit reduced salivation and mucus formation, which decreases the normal microflora of the oral cavity and makes the oral cavity more vulnerable to pathogens such as Aspergillus species.

This reduced salivation may also allow pathogens to accumulate in the supragingival and subgingival areas, thus increasing periodontal inflammation in gutkha chewers compared to non-chewers. (Javet et al. 2008, Mavropoulos et al. 2001, Avasn et al. 2004, Tseng et al. 2008, Liu et al. 2006, Ohnishi et al. 2009, Shevalye et al. 2012, Javet et al. 2012)

Javed, 2015 conducted a study with the aim of evaluating the clinical periodontal parameters and the levels of IL-1β, IL-6, MMP-8 and MMP-9 in total saliva in patients who habitually chew gutka and non-consumer patients. Forty-five gutka chewers and forty-five control subjects were included.

The researchers recorded periodontal parameters, including plaque index (PI), bleeding on probing (BOP), probing depth (PD) > 3 mm, clinical attachment loss (AL), marginal bone

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loss (MBL) and the number of missing teeth. The authors established that periodontal inflammatory conditions worsen, and levels of IL-6, IL-1β, MMP-8, and MMP-9 in saliva were higher among gutka chewers than nonchewers. This finding is consistent with previous studies conducted by Nair et al. 1990, Jeng et al. 1999, and Javet et al. 2008, these authors suggested that slaked lime (aqueous calcium hydroxide), an essential ingredient in gutka, is associated with oral mucosal inflammation.

Furthermore, extracts from areca nut, which contains arecoline as the main component, have been found to inhibit the growth of cultured gingival keratinocytes and periodontal fibroblasts. These results may help explain why gutka-chewers experience more severe periodontal conditions and oral symptoms than non-chewers.

Previous studies have stated that the effect of smoking and ST use on the periodontal status can be reasoned on two factors: alterations in host tissue and response of periodontal flora. (Warad et al. 2014) Also, the occurrence of gingival recession has been associated with site placement of ST product in the oral cavity. (Ahad et al. 2021) The most common reason given by users was peer pressure, general stress, and advertisements. The studies have proven that young people are the most liable to this addiction.

Methods to quit this habit should be implemented by health workers, relatives, and the community. (Anand et al. 2021)

Conclusion

With the articles investigated, we conclude that the consumption of tobacco has taken a huge toll worldwide. The widespread of ST products such as gutkha and paan masala has affected all age groups. It is clear that the habit of using tobacco without smoking produces results that are distinct from those resulting from the sole application of any one habit.

Even with the worst levels of oral hygiene, those with this behavior showed the least amount of gingival irritation. People with the frequent habit had significantly more teeth with gingival recession than any other group, although having slightly shallower periodontal pockets overall. Therefore, it would seem that stopping the use of smokeless tobacco in Asia should be given top priority in order to prevent periodontal disease. Oral cancer rates are increasing due to the use of smokeless tobacco products, especially among the lower socioeconomic levels. It is crucial to reduce the adverse health effects, by improving public health campaigns and enhancing the access for the affected individuals.

Therefore, programs should be implemented to control the use of ST products, and to establish appropriate data management, monitoring, and to evaluate health systems.

Conflicts of interest:

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