REVIEW ARTICLE

Ameliorative role of phytochemical against smokeless tobacco products (STP) induced gastrointestinal health: An overview

Merina Yasmin, Sandip K Sinha*

ABSTRACT

Background: Medicinal plants include phytochemicals that help treat a variety of illnesses, including those affecting the digestive system. Gutkha and other smokeless tobacco products can harm the esophagus, stomach, intestines, and mouth. *Aims and Objectives:* Citrus Medica, Clove, Fennel, Ginger, and Andrographis are among the phytochemicals that may lessen the effects of STP on the GI system, according to studies. This review aims to determine how these medicinal herbs can help avoid GI issues brought on by STP. *Materials &methods:* We conducted this instructive study using several online resources, including PubMed, Web of Science, and Scopus journal listings, were used to perform this instructive study. We began by summarizing the numerous forms of STP and its general health concerns in light of the various medicinal herbs that are particularly effective in preventing health damage associated with STP. *Results:* Several tobacco-specific nitrosamine components (NNN, NNK, TSNA, etc.) found in various ST product types induce cancer in various bodily organs and are the source of several organ-specific (GI system) illnesses. Medicinal plants have a powerful effect on the digestive system. *Conclusion:* According to the study's findings, STP affects the entire gastrointestinal system and individual organs, and most plant-based bioactive substances can effectively prevent these harms.

Keywords: Tobacco, Nicotine, GI tract, Medicinal plants, Phytocompounds

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INTRODUCTION

Snuff and chewing tobacco are examples of smokeless tobacco products (STP) from unburned tobacco. Chewing comes in the form of twists, plugs, or loose leaves. It is situated between the cheek and the teeth or gums. Another is finely powdered tobacco snuff. It is available for purchase, wet or dry. The most common type of wet snuff is a packet. There is also dried snuff powder. Other forms of STP include sticks, pellets, film strips, and ariva. In Western countries, conventional smokeless tobacco is usually used as chewing tobacco in products like plugs, rolls, twists, and snuff dips. It can be either dry (containing less than 10% water) or moist (containing 40–60% water). The Mayo Clinic states that chewing tobacco is a common source of secondhand smoke (STP). It also contains nicotine and other ingredients that most people find addictive. Various nations have varying rates of young people (males) using smokeless tobacco products, according to data from the Global Youth Tobacco Survey (GYTS), which was carried out between 2011 and 2016: 2.1% in Indonesia, 23.2% in Bhutan, 0.5% in Sri Lanka, and 19.8% in Bhutan (females)[1].To guard against the detrimental effects of STP on the GI tract (oral lesion, oesophageal cancer, liver damage, gastric ulcer, peptic ulcer, inflammatory bowel disease, gallbladder), we try to identify the different phytochemicals from medicinal herbs because they are more effective than traditional medicine and have fewer side effects. These effects of the hooked population can be lessened by the many medicinal plants that are present in our immediate environment. Most medicinal plants have been used to treat a variety of illnesses due to their pure or bioactive ingredients. Plant-based natural ingredients have been used to create a variety of therapeutic medications. These days, it's quite difficult to compare phytochemicals to traditional therapy. Since ancient times, the efficacy of phytochemicals for therapeutic purposes has been generally acknowledged. The secondary metabolites of therapeutic plants have potent antibacterial effects against harmful bacteria like *Staphylococcus aureus* and *Bacillus cereccus*, in addition to their antimicrobial qualities.[2] Thus, the objective of this review endeavor is to develop a current health database that considers how STP is used by the general public and any prospective advantages that medicinal plants might have for averting STP-related health problems.

Department of Human Physiology, Vidyasagar University, Midnapore.

***Corresponding author:** Sandip K Sinha, Department of Human Physiology, Vidyasagar University, Midnapore, Email: sandipkrsinhavu@gamil.com

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METHODS AND MATERIALS

Throughout this review procedure, we make an effort to gather all the information from numerous websites and search engines, including NCBI, PubMed, NCBS, Elsevier,

Web of Science, Scopus Journal List, etc. These products and information were also produced concurrently using a variety of other sources, such as newspapers, specialist websites, survey-based data, and media news.

Different types of smokeless tobacco products

People of all socioeconomic backgrounds in our country use traditional STPs. These days, STP can take many forms, such as toombak in Sudan, snuff in South Africa, Maras's powder in Turkey, and homemade iqmik in Alaska. Several varieties are found in Central, South, and Southwest Asia, including betel-nut quid, pan masala, shammah, alqat, nass, naswar, khaini, mishri, zarda, mawa, gutkha, bajjar, and gadakhu[3] used a range of chemicals in tobacco products, including menthol, oils, molasses, slaked lime, areca nut, spices, catechu, and other colorings and scents.[3,4] The most common type of STP among hospital staff and the general people in Pakistan is gutkha[5]

General health effects of STP

There is a deadly element in every tobacco product. There are around thirty different types of carcinogenic chemicals in STP. Approximately 7000 chemicals make up water pipes overall, 250 of which are commercially available and known to be harmful or carcinogenic. Because tobacco includes carcinogenic substances that cause a variety of detrimental health effects, including tongue lesions, oesophageal lesions, leukoplakia, periodontitis, and other oral lesions, STP use greatly increases the burden of oral disease. Significant facial disfigurement and the inability to swallow, chew, and speak (voice loss) are two outcomes of oral cancer that have been demonstrated in several nations.STP use increases the risk of head and neck cancers, such as oesophageal, laryngeal, and pharyngeal cancers. Patients suffer from unbearable pain and are consequently unable to eat. It also affects the cardiovascular system, which can result in strokes and heart attacks. ST causes oral, oesophageal, and pancreatic cancer in humans [6].

In addition to animal models, TSNA has been identified in ST products and malignancies affecting the liver, pancreatic, trachea, nasal cavity, and lung as a major cause of cancer. Benzopyrene, formaldehyde, acetaldehyde, nickel, and cadmium are also present in chewing tobacco. This is the cause of pancreatic, oesophageal, and stomach cancer. STP contains addictive chemicals and nicotine. For this reason, it is not safer than smoking. Some groups of people use smokeless tobacco regularly. Regular use of STP can have detrimental implications on one's health. These products are usually regularly consumed by sucking, swallowing, or chewing them. These items truly appeal to the broad population (people of all genders) because of their high addiction. Cotinine and nicotine, two of the active components in many STPs, are responsible for their toxicological effects. Additionally, the long-term use of STP by smokers showed dental caries, gingivitis, gum disease, oral candidiasis, and periodontal diseases [7]. Furthermore, it was demonstrated that there was a significant decrease in serum activity and impairment in the function of salivary enzymes, namely salivary-α amylase activity, which is essential for preserving good oral health [8]. The risk of death and illness from tobacco smoking ranks second, per a survey-based study done on a rural community in India. Just 1.5% of them are women, and 61.2% of them are men who use tobacco products. 81.7% of tobacco users smoked, 6.5 % used smokeless tobacco, and 11.8% used both types of tobacco [9].

Based on the preceding review, we can ascertain how STP affects the cardiovascular, reproductive, immune, and dental systems (Table 1). Free radical levels, the risk of pylori infection, stomach motility, duodenogastric reflux of bile salts, and the generation of acid and pepsin can all be increased by nicotine exposure. Additionally, prostaglandin, mucus formation, stomach mucosal blood flow, and the therapeutic efficacy of H2 receptor antagonists are all decreased by nicotine [10]. As a result, STP also affects gastrointestinal health, including pancreatic disorders, inflammatory bowel disease, liver and gall bladder disorders, and peptic ulcers. It affects dental health as well. We may be attempting to make the case that all smokeless tobacco products are hazardous because of their toxic active ingredient, which seriously disrupts our normal physiological processes. The following health effects are linked to chewing tobacco (snuff, snus, naswar, gul, zarda, gutkha, mawa, and betel quid areca nut): cancers of the esophagus, lip, oral cavity, larynx, and nasopharynx, and IHD, according to a systematic study with meta-analysis to generate conservative risk regarding the chewing form of STP [11]. Numerous prior studies have already established that STP has a range of detrimental effects on health. However, nothing is known about how STP affects gastrointestinal health. Thus, this review's objective is to discover different gastrointestinal health issues linked to long-term use of smokeless tobacco products.

Epidemiology of GI tract

STP has a major impact on the GI tract, according to numerous studies (Table 1). To create SLT products, tobacco is grown on 14% of India's land. The number of people who chewed tobacco increased from 722 million in 1990–1991 to 15 times more in just ten years. The combined effects of betel quid and areca nut consumption cause most pharyngeal malignancies (nasopharynx, oropharynx, hypopharynx, and pharynx), as well as cancers of the esophagus, larynx, liver, stomach, cervix, colon, and gall bladder. Among these several cancer types, using tobacco and betel quid together also increases the risk of developing cancer [6]. More than 10% of Indian women aged 15 and older utilized alternative smokeless tobacco and white paper (12.8%) in 16 Indian states. Furthermore, exposing fetuses to the chemicals and risks present in smokeless tobacco products during pregnancy and lactation leads to preventable morbidities and adverse outcomes because the nicotine in these products acts as a neuro-teratogen, affecting the development of the fetus's brain, lungs, and CNS; it also crosses the placental barrier

Table 1: Shows different types of STP and its related diseases

Name of STP	*Health effect/ disease name*
Shammah	Dental disease, oral cancer, oesophagus cancer, and pancreas cancer. Cardiovascular effects such as increased heart rate and blood pressure, myocardial infarction, stroke, and ischemic heart disease Reproductive effects include stillbirth, low birth weight, and premature birth. [12-16]
Snus	Gastric cancer, squamous cell cancer, cardiac cancer, oesophageal cancer[17,18]
Paan Masala	Hyperkeratosis, edema, Dysplasia, malignant tumor, neoplasia, ovarian cysts, kidney inflammation. [19,20]
Betel quid and Areca nut	Oral and stomach cancer Liver and oesophageal cancer. [4,21,22]
Gutkha	Oral carcinoma, oral submucous fibrosis (OSF) Lower testosterone level, reduced body and organ weight. [23, 24]
Piper betel leaf	Oral squamous cell carcinoma (OSCC), verrucous carcinoma of the tongue (VCC), oral potentially malignant disorders (OPMD), Leukoplakia, Erythroplakia, and OSMF. [25]
White paper	Oral and pharyngeal cancer, Oesophageal cancer, Upper Aero Digestive Tract cancer (UADT), Cervical cancer and ischemic heart diseases (IHD). [26]

[26]. In 2009, GYTS found that 7.5% of girls and 10.7% of boys in India between the ages of 13 and 15 utilized some form of SLT. SLT is currently issued by 18% of women and 33% of men. Because snuff and chewing tobacco are so common in India, oral cancers account for 70% of all fatalities there. Other cancers caused by tobacco use include those of the stomach, intestines, pharynx, larynx, esophagus, nasal cavity, pancreas, and urinary system. This condition also affects the gastrointestinal tract [27], which lowers stomach pH (usually between 2.3 and 3.5) and increases gastric acid production in addition to the mouth lesion caused by chewing or snuffing tobacco. Inflammation of the colon, diarrhea, and abdominal pain are also possible. Infection of the upper gastrointestinal tract caused by H. pylori. Due to the use of snus, the squamous epithelium at the esophageal-gastric junction has been associated with esophagogastroduodenoscopy (73.3%), basal cell hyperplasia (95%), elongation of papillae (95%), peptic ulcer diseases (95%), and gastrointestinal symptoms (74.2%).[28] Snus is consumed by 900,000 individuals in Sudan. Compared to 21% of males and 4% of women, 13% of men and 17% of women use cigarettes. A national US survey found that 9% of male college students and 0.4% of female students use snus. Inflammation, a 46% higher risk of pancreatitis, and an increased frequency of stomach cancers were all observed in STP users. Smokeless tobacco use increases the risk of periodontal diseases, oral mucosal changes at the placement site in the mouth cavity, and local irritant effects that ultimately lead to gingival inflammation, according to a cross-sectional survey conducted among men in North India, whose average age group is 11 years old [29]. Smokeless tobacco products (Shammah, tombak, gutkha, betel quid, and dry snuff) sold all over the world include many carcinogenic chemicals that have been associated with an increased risk of mouth cancer. [30]. In comparison to those who never use tobacco, individuals who use snus, a popular smokeless tobacco product, both men and women, have an unhealthy eating pattern in Scandinavia, which may be a risk factor for cardiovascular diseases (CVD) [31]. This was found in a population-based cross-sectional study.

Antagonistic effects of different medicinal plants against STP

Over time, medicinal plants have developed into a distinct source of bioactive compounds (Table 2). Plants of all kinds are easily accessible in our immediate environment since their therapeutic potential has been extensively studied for a long time [35]. These days, many medicinal plants are always the best alternative to pharmaceuticals because they have fewer negative effects than any other chemical component. As a result, we can easily extract the vital bioactive compounds from different plant parts. It has been demonstrated that the plant's separated secondary bioactive compounds are more physiologically effective at shielding mammalian systems from a variety of toxins. In this study, we seek to gather pertinent studies on medicinal herbs and their effects on the gastrointestinal tracts of mammals. Some medicinal herbs can decrease the effects of nicotine on the gastrointestinal tract because of their laxative and anti-diarrheal qualities. Increased intestinal secretion, motility, absorption rate, and transient stimulation with preservation of peristaltic movement are some of these characteristics [36]. Furthermore, clove oil has a powerful effect on the digestive system by reducing diarrhea, gastric irritation, peptic ulcers, and stomach gas pressure [37]. Fennel plants have a significant protective effect against gastrointestinal illnesses, reduce the risk of gastric ulcers, and enhance the stomach's mucosal lining, according to [38]. As a result, we are also trying to develop a schematic showing many medicinal plants, their active ingredients, and the organs essential to the gastrointestinal tract.

Table 2: List of different medicinal plants and their active compound responsible for protective effects in several areas of GI tract

Plant name		*Active part*	*Active compound*	*Effective organ and tissue*
Fennel (*Foeniculum vulgare*)[38]	 [a]	Fruits and seeds oil	Anethole	Stomach and G.I. tract
Ginger (*Zingiber officinale*)[39]	 [b]	Ginger oil (rhizome)	Sesquiterpene	Intestine and Gastric mucosa
Caraway (*Carum carvi* L.)[40]	 [c]	Seeds	Carvol and Carvene	Stomach
Sweet flag/ sweet calomel (*Acorus calamus*)[40]	 [d]	Rhizomes	Alkaloids	Intestine
Golden apple / wood apple (*Aegle marmelos*)[40]	 [e]	Leaves	Alkaloids, terpenoids, saponins	Stomach
Aloe Vera (*Aloe barbadensis*)[40]	 [f]	Leaf	Vit A, C, E, carotenoids	Intestine and its wall
Green chiretta (*Andrographis paniculata*)[40]	 [g]	Whole plant	Diterpenes and lactones	Intestine
Papaya (*Carica papaya*)[40]	 [h]	Leaves	Terpenoids, Saponins, Tannins	Stomach
Pipe tree (*Cassia fistula*)[40]	 [i]	Bark	Flavonoids	Intestinal part
Golden eye grass (*Curculigoorchioides*)[40]	 [j]	Rhizomes	Alkaloids, flavonoids	Stomach
Turmeric (*Curcuma longa*)[41]	 [k]	Rhizome	Curcumin	Intestine
Lemon (*Citrus medica*)[42]	 [l]	Fruits	Flavonones and Isolimonone	Stomach and Intestine

Clove (*Sygyzium aromaticum*)[43]	 [m]	Flower bud	Eugenol	Intestine
Ogala/ Asunmon[44]	 [n]	Dried leaves	Flavonoids	Intestine

Image Sources: [a] https://www.amazon.in/Kitchen-Jungle-Green-Fennel-Seeds/dp/B08JKPQCZB; [b] https://www.allrecipes.com/article/what-is-ginger/ [c] https://www.nutrition-and-you.com/caraway-seed.html [d] https://www.fs.usda.gov/wildflowers/plant-of-the-week/acorus_americanus.shtml [e] https://suyashayurveda.com/product/wood-apple-oil/ [f] https://www.flipkart.com/bee-green-aloe-vera-plant/p/itm8a8fd646a72ca?pid=PSGG73FW6H7NGZHY. [g] https://wcc.edu.in/andrographis-paniculata/. [h] https://healthybuddha.in/papaya-small [i] https://www.amazon.in/Creative-Farmer-Garden-Fistula-Kanikkonna/dp/B08P5QTFB7 [j] https://www.facebook.com/photo.php?fbid=1551843631556754&id=1415537775187341&set=a.1478768742197577&locale=mt_MT [k] https://www.dmtraders.com/product/turmeric-powder-manjal-podi/. [l] https://farmsbazaar.com/fresh-lemon-farmfresh-vegetable-hydroponics-inhydro-farmsbazaar [m] https://tinyurl.com/39ps94nt [n] https://www.cabidigitallibrary.org/doi/full/10.1079/cabicompendium.117090

Types of medicinal plants against STP

Many gastrointestinal and digestive diseases can be prevented and treated with a variety of phytochemicals and nutraceuticals found in medicinal plants. The findings of this study showed that 14 medicinal plants had beneficial effects on different gastrointestinal tract organs because of their bioactive components (Table 2). Sesquiterpene is an important bioactive component of ginger oil that helps maintain the stomach mucosa layer [39]. It has been demonstrated that terpenoid flavonoids, which are present in the leaves and fruits of papaya, lemon, golden apple, pipe tree, and sweet flag plants, have positive effects on the gastrointestinal tract's stomach and intestines [40]. These plants' rhizomes and leaves contain alkaloids that likewise have this effect.

DISCUSSION

As mentioned earlier in the review study, the results indicate that a wide range of phytochemicals with numerous health advantages can be extracted from medicinal plants. These phytochemicals are very beneficial in treating common illnesses in people because the majority of herbal sources are affordable and easily accessible in our community. Numerous scientific research has demonstrated that while herbal medicine is more advantageous and easily accessible at a cheaper cost for treating various conditions, traditional medicine has serious drawbacks. We have included some active chemicals derived from various active plant components (leaf, root, stem, bark, etc.) to provide specific disease protection. It has been demonstrated that some plants, including fennel seeds, caraway seeds, and papaya leaves, have stomach-healing properties. On the other hand, it has been demonstrated that several popular STPs, like snus, paan masala, and snuff, have extremely negative effects on the stomach and other gastrointestinal tract areas [28,33]. On the other hand, turmeric's rhizome contains curcumin [41]. Aloe vera leaves contain carotenoids [20], the entire Andrographis plant still contains lactones and diterpenes [40], and the rhizome of ginger contains sesquiterpenes [43]. These phytochemicals are all protected from the negative effects of STP on the digestive system.

SUMMARY

The purpose of this review is to demonstrate the impact of STP on the gastrointestinal tract as well as the protective and therapeutic function of phytochemicals. The majority of phytochemicals are useful in treating gastrointestinal disorders as well as complicated medical illnesses of any kind. This study illustrates how many forms of STP may affect our G.I. health and many organs directly or indirectly. Phytochemicals, the active components of plants, are essentially in charge of the recovery from gastrointestinal illnesses brought on by STP.

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PEER-REVIEWED CERTIFICATION

During the review of this manuscript, a double-blind peer-review policy has been followed. The author(s) of this manuscript received review comments from a minimum of two peer-reviewers. Author(s) submitted revised manuscript as per the comments of the assigned reviewers. On the basis of revision(s) done by the author(s) and compliance to the Reviewers' comments on the manuscript, Editor(s) has approved the revised manuscript for final publication.