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Review Article

MONOGRAPH OF TOBACCO (NICOTIANA TABACUM)

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Tobacco plant with flowers

ABSTRACT

The use of tobacco dates back to the ancient civilizations of the Americas, where it played a central role in religious occasions. The peoples smoked tobacco in cigars and pipes and chewed it with lime, for its pleasurable euphoriant effects. In the 16th century, Europeans spread the use of tobacco in North America, while the Spanish bring it into Europe. In the 1559, Jean Nicot, the French ambassador to Portugal, wrote about the medicinal properties of tobacco and sent seeds to the French royal family, and promoted the use throughout the world. Because of his great work on tobacco plant, his name was given to its genus, *Nicotiana*, and its active principle, nicotine. The Materia Medica of India provides a great deal of information on the Ayurveda, folklore practices and traditional aspects of therapeutically important natural products tobacco one of them. Tobacco is processed from the leaves of plants in the genus i.e. *Nicotiana*. Nicotine tartrate used as a pesticide as well as in medicines. It is commonly used as a cash crop in countries like India, China, Cuba and the United States. Any plant of the genus Nicotiana of the Solanaceae family is called tobacco. The tobacco products are manufactured from the leaves, cured & dried and used in cigars and cigarettes, snuff, and pipe and chewing tobacco. Tobacco plants are also used in bioengineering and as ornamentals plant. The pharmacological activities of *Nicotiana tabacum* is mostly due to its content of nicotine which stimulates the nicotine receptors leading to release of substances such as acetylcholine, nor-epinephrine, dopamine, serotonin, vasopressin and growth hormone. Nicotine is a major component of tobacco has been demonstrated to accelerate angiogenesis and wound healing in genetically diabetic mice. The ethnomedical uses include the use of the decoction of leaves as antispasmodics, diuretics, emetics, expectorants, sedatives, and in rheumatic swellings, anesthetics, antibacterial, antimicrobial, anthelmintic, anticonvulsants and for anti-fungal activities. Other use includes; treatment of asthma by Indians, treatment of worms in Africa, treatment of wounds in Columbia and treatment of dysmenorrheal in Cuba among others. The plant *Nicotiana tobaccum* also have the great activities on peripheral nervous system, central nervous system, cardiovascular system, gastrointestinal tract, exocrine glands, Hematopoietic system, algesia, Alzheimer and on body weight.

KEY WORDS: Tamakhu, Snuff, Chewing tobacco, Smoking tobacco.

INTRODUCTION

Tobacco plant is a perennial, erect glandular-pubescent herb and found only in cultivation. *Nicotiana tabacum* is basically native of America but it is now commercially cultivated throughout the world. The other varieties of tobacco plant are cultivated as ornamental plants or grow as a weed. *Nicotiana tabacum* is a robust annual little branched herb grows to heights between 1 to 2 meters, with large green leaves, oblong-lanceolate, acuminate, the lower semiamplexicaul and decurrent and long trumpet shaped white-pinkish, rosy or reddish

flowers, pedicelled, 4-5 cm long, in many-flowered, usually panicled racemes. Capsule 1.5-1.8 cm long, a little longer than the calyx. All parts of herb are sticky, covered with short viscid-glandular hairs, which exude a yellow secretion that contain alkaloid known as nicotine.

TAXONOMIC CLASSIFICATION

Scientific name: Nicotiana Tabacum Linn.
Kingdom: Plantae, Eudicots, Asterids
Order: Solanales
Genus: *Nicotiana*
Species: *Nicotiana tabacum*
Division: Magnoliophyta
Class: Magnoliopsida
Family: Solanaceae
Latin names: *Nicotiana tabacum*
Common names: Fumo, Petume, Petina, Pitura, Etum, Tabaco, Tobacco, Tabaci Folia.
Synonyms: Tabacca, Tabaci Folia, Tobacco, Tamak, Siah (Marma).
Habitat: Virginia, America, China, Turkey, Greece, Holland, France, Germany and most sub-tropical countries.

Tobacco flowers & seeds

Tobacco leaves

Tobacco cultivation

LIST OF *NICOTIANA TOBACUM* SPECIES (Clausen, 1928; Johannes et al., 2002; Chase et al., 2003; Knapp et al., 2004)

The genus tobacco includes more than 7 0 species with variable biological activities and most of them are indigenous to America. *Nicotiana tabacum*, the plant now used for commercial tobacco production, is probably of South American origin. The *Nicotiana rustica* and the other species are native of North America. Both species are found distributed from Florida to New Mexico, to Massachusetts, New York, Southern Ontario and Minnesota. *Nicotiana tabacum* has a uniquely high proportion of alkaloids i.e. nicotine and is considered to have survived as a species by man's protection. Apart from this there are other varieties cultivated commonly like *Nicotiana affinis; Nicotiana rustica; Nicotiana Sanderae; Nicotiana alata grandiflora; Nicotiana acuminata; Nicotiana Bigelovii (Indian Tobacco); Nicotiana longiflora; Nicotiana noctiflora; Nicotiana suaveolens; Nicotiana sylvestris; Nicotiana Tabacum; Nicotiana*

wigandioides etc. In 1559, tobacco is called nicotiana in honour of Jean Nicot, who finds medical uses for tobacco. Tobacco cultivation has a history of about 8000 years. Portuguese traders introduced tobacco in India around during 1600. Tobacco's medicinal as well as intoxicating properties facilitated its easy assimilation into cultural and rituals of many societies (Feinhandler et al., 1979). The species may be classified on the bases of way to use as:-

(a) Traditionally used as smoking tobacco

Nicotiana acuminata (Graham) Hook.
Nicotiana africana Merxm.
Nicotiana alata Link & Otto
Nicotiana ameghinoi Speg.
Nicotiana amplexicaulis N.T. Burb.
Nicotiana arentsii Goodsp.
Nicotiana attenuata Torrey ex S. Watson
Nicotiana azambujae L.B. Smith & Downs
Nicotiana benavidesii Goodsp.
Nicotiana bigelovii
Nicotiana persica
Nicotiana trigonophylla
Nicotiana mutafloria
Nicotiana angustifolia
Nicotiana mexicana
Nicotiana pusilla
Nicotiana acaulis Speg
Nicotiana bonariensis Lehm.
Nicotiana burbidgeae Symon
Nicotiana cavicola N.T. Burb.
Nicotiana clevelandii A. Gray
Nicotiana cordifolia Phil.
Nicotiana corymbosa J. Rémy
Nicotiana cutleri D'Arcy
Nicotiana debneyi Domin
Nicotiana excelsior J.M. Black
Nicotiana exigua H.M. Wheeler
Nicotiana forgetiana Hemsl.
Nicotiana fragrans Hooker
Nicotiana glauca Graham
Nicotiana glutinosa L.
Nicotiana goodspeedii H.M. Wheeler
Nicotiana hesperis N.T. Burb.
Nicotiana heterantha Kenneally & Symon
Nicotiana kawakamii Y. Ohashi
Nicotiana knightiana Goodsp.
Nicotiana langsdorffii Weinm.
Nicotiana linearis Phil.
Nicotiana longibracteata Phil.

(b) Traditionally used as chewing/quiding/spit tobacco

Nicotiana gossei Domin
Nicotiana ingulba J.M. Black
Nicotiana benthamiana Domin

(c) Manmade hybrids species

Nicotiana × didepta N. debneyi × N. tabacum
Nicotiana × sanderae Hort. ex Wats. N. alata × N. forgetiana
Nicotiana × digluta N. glutinosa × N. tabacum
Nicotiana longiflora Cav.
Nicotiana maritima H.M. Wheeler
Nicotiana miersii J. Remy
Nicotiana mutabilis Stehmann & Samir
Nicotiana nesophila I.M. Johnston
Nicotiana noctiflora Hook.
Nicotiana nudicaulis S. Watson
Nicotiana obtusifolia M. Martens & Galeotti
Nicotiana occidentalis H.M. Wheeler
Nicotiana otophora Griseb.
Nicotiana paa Mart. Crov.
Nicotiana palmeri A. Gray
Nicotiana paniculata L.
Nicotiana pauciflora J. Remy
Nicotiana petuniodes (Griseb.) Millan.
Nicotiana plumbaginifolia Viv.
Nicotiana quadrivalvis
Nicotiana raimondii J.F. Macbr.
Nicotiana repanda Willd.
Nicotiana rosulata (S. Moore) Domin
Nicotiana rotundifolia Lindl.
Nicotiana rustica L.
Nicotiana setchellii Goodsp.
Nicotiana solanifolia Walp.
Nicotiana spegazzinii Millan
Nicotiana stenocarpa H.M. Wheeler
Nicotiana stocktonii Brandegee
Nicotiana suaveolens Lehm.
Nicotiana sylvestris Speg.
Nicotiana tabacum L.
Nicotiana thrysiflora Bitter ex Goodsp.
Nicotiana tomentosa Ruiz & Pav.
Nicotiana tomentosiformis Goodsp.
Nicotiana truncata D.E. Symon
Nicotiana umbratica N.T. Burb.
Nicotiana undulata Ruiz & Pav.
Nicotiana wigandioides Koch & Fintelm.
Nicotiana wuttkei Clarkson & Symon
Petunia axillaris (Lam.) Britton et al.

Nicotiana simulans N.T. Burb.
Nicotiana megalosiphon Van Huerck & Mull. Arg.
Nicotiana tobacum L.
Nicotiana velutina H.M. Wheeler

Nicotiana tabacum is the Latin name for the tobacco plant. Originally, *Nicotiana tabacum* came from North and South America, but it is now grown almost all over the world. The plant is easy to grow, used as an ornamental plant and for making tobacco. To obtain high yield of tobacco, remove the side shoots and flowers, so that the leaves of the plant grow well. The germination of the tobacco seeds can be start during early spring session. Place couple of seeds at a time in a pot with soil and covering with transparent plastic so that the humidity remains high. Within 7 days the first seeds will start to germinate. After a few weeks can move the plants to a bigger pot. Place the plants in the sun light and prevent from wind. Indoors the plant are not exceed one meter, but outdoors it can reach up to three meters high. The tobacco flowers are white and pink, blooms from July to September in the year. The plant is virtually impervious to diseases and pests. The main commercial species of tobacco like *Nicotiana tabacum,* is believed native to America, like most tobacco plants, but has been so long cultivated that it is no longer known in the wild. *Nicotiana rustica,* a mild-flavored, fast-burning species, was the tobacco originally raised in Virginia, but it is now grown chiefly in Turkey, India, and Russia. The alkaloid nicotine is the most characteristic constituent of tobacco and is responsible for its addictive nature (Jahn, 2002). The possible harmful effects of the nicotine, tarry compounds, and carbon monoxide in tobacco smoke vary with the individual's tolerance.

Nicotiana tabacum, or cultivated tobacco, is a perennial herb. It is found only in cultivation, where it is the most commonly grown of all plants in the *Nicotiana* genus, and its leaves are commercially grown in many countries to be processed into tobacco. Research is ongoing into its ancestry among wild *Nicotiana* species, but it is believed to be a hybrid of *Nicotiana sylvestris*, *Nicotiana tomentosiformis*, and possibly *Nicotiana otophora* (Nan Ren and Michael, 2001). The tobacco plant, *Nicotiana tabaccum*, has probably been responsible for more deaths than any other herb. Present, irrational tobacco use is causing over 3 million deaths a year worldwide, and if current trends continue the annual mortality will exceed 10 million by around 2030 (Peto et al., 1996; Reddy and Gupta, 2004; Charlton, 2004). The history of the medicinal use of tobacco before the Civil War has apparently not been documented. Review of publications on the tobacco shows that this plant was long used as orthodox medicine by the medical profession. The peoples of North America, throughout use traditional tobacco plants for spiritual, ceremonial and therapeutical purposes goes back thousands of years. An extensive work has been done on the principle chemical constituents of various plants of tobacco. Tobacco and tobacco smoke constituents, lists a large number of compounds which have been isolated from it (Stedman, 1968; Roberts and Rohde, 1972). The chief chemical constituents identified and isolated are nicotine, nornicotine, anabasine, myosmine, anatabine, nitrate and sorbitol (Fowles, 2003) . Apart from these, tobacco also contains nicotinic acid, nicotelline (Leete, 1983) nicotianine (Noguchi et al., 1968) etc.

HISTORY

The written history of tobacco begins in the year 1492 when Christopher Columbus discovered American Indians treating their ills with leaves of an herb which he had never seen before. After that in 1536, European travelers to the New World carried home a considerable body of medical knowledge concerning the plant, acquired from Native American laymen, medicine men, and physicians in many parts of the Western Hemisphere. This knowledge was quickly spread by word of mouth and by books published and circulated throughout Western Europe. The result was that Western European physicians adopted tobacco as medicine. Natural occurrence of nicotiana is restricted to the American continent, Australia and the South Pacific. The majorities are confined to South America and this, with other geographical evidence suggests a South American origin for this genus. *Nicotiana tabacum* originated from the borders of Argentina and Bolivia (Akehurst, 1968).

The genus derives its name from Jean Nicot, a Portuguese who introduced the Tobacco plant into France. The specific name being derived from the Haitian word for the pipe in which the herb is smoked. The use of tobacco originated among the indigenous inhabitants of the Western Hemisphere in pre-Columbian times. Tobacco was introduced into Spain and Portugal in the mid-16th century, initially for its supposed virtues as a panacea. It spread to other European countries and then to Asia and Africa, where its use became general in the 17th century. The first tobacco to reach England was probably a crop harvested in Virginia, where John Rolfe (1954) experimented with Spanish types of tobacco seed and introduced tobacco as a crop as early as 1612. By 1619 tobacco had become a leading export of Virginia, where it was later used as a basis of currency. The tobacco plant was introduced into England by Sir Walter Raleigh and his friends in 1586, and at first met with violent opposition. Kings prohibited it, Popes pronounced against it in Bulls, and in the East Sultans condemned tobacco smokers to cruel deaths. Three hundred years later, in 1885, the leaves were official in the British Pharmacopoeia. In their first

voyage to the new world, Christopher Columbus and his expedition were introduced to a plant whose smoke was called *tobacco* by the natives of Hispaniola. In 1560, Jean Nicot de Villemain brought tobacco seeds and leaves as a wonder drug to the French court. In 1586 the botanist Jaques Dalechamps gave the plant the name of *Herba nicotiana*, which was also adopted by Linne. It was considered a decorative plant at first, then a panacea, before it became a common snuff and tobacco plant. Tobacco arrived in Africa at the beginning of the 17th century. The leaf extract was a popular pest control method up to the beginning of the 20th century. In 1851, the Belgian chemist Jean Stas was the first to prove the use of tobacco extract as a murder poison in the civilized world. The Belgian count Hippolyte Visart de Bocarme had poisoned his brother-in-law with tobacco leaf extract in order to acquire some urgently needed money. This was the first exact proof of alkaloids in forensic medicine (Wennig, 2009). Rodrigo de Jerez, a Spanish explorer, brought tobacco back to Spain in the early 1500's, where the habit of smoking became popular very quickly. As it became more popular, its value skyrocketed, and tobacco was used as money in the early American Colonies. Snuff use was very popular in 18th Century, but by the 19th century cigars had become the primary tobacco product. In the mid-1800s, Philip Morris, J.E. Liggett, and R.J. Reynolds began their tobacco companies. Then came the invention of matches and cigarette rolling machines. Cigarette use began to skyrocket. During World War I soldiers were provided with free cigarettes. Between 1910 and 1920, per capita consumption of cigarettes increased from 94 to 419 per year. The link between cigarette smoking and cancer was already evident. In 1930, the lung cancer rate for white men in the United State was 4.9 per 100,000. By 1948, the rate had increased to 27.1 per 100,000. The rapid increase in smoking and its health consequences led congress to mandate in 1965 that a Surgeon General's warning appear on every pack of cigarettes. In the 1970's, airlines began offering non-smoking sections on flights, and smoking was prohibited in many public spaces. In the 1980's, research revealed that secondhand smoke, as well as smokeless tobacco, has serious health consequences, including cancer. The 1990's saw a great deal of legal action taken against the major tobacco companies as well as numerous campaigns to inform the public about the dangers of smoking. In 1999, the Philip Morris Tobacco Company recognized that there is an overwhelming medical and scientific consensus that cigarette smoking causes lung cancer, heart disease, emphysema and other serious diseases in smokers... there is no safe cigarette... cigarette smoking is addictive. Around this time, major tobacco companies began to confess to the fact that they had been focusing their advertising campaigns toward young people (Borio, 2010).

DESCRIPTION & DISTRIBUTION

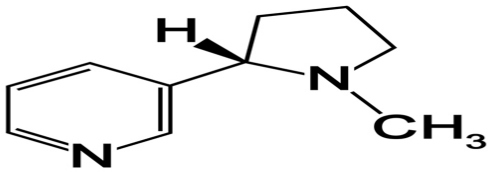
Tobacco is an annual, long fibrous root, stem erect, round, hairy, and viscid; it branches near the top and is from 3 to 6 feet high. Leaves large, numerous, alternate, sessile, somewhat decurrent, ovate, lanceolate, pointed, entire, slightly viscid and hairy, pale-green color, brittle, narcotic odor, with a nauseous, bitter acrid taste. Nicotine is a volatile oil, inflammable, powerfully alkaline, with an acrid smell and a burning taste. By distillation with water it yields a concrete volatile oil termed nicotianin or tobacco camphor, which is tasteless, crystalline, and smells of tobacco; other constituents are albumen, resin, gum, and inorganic matters. It has been cultivated in pre Columbian times in the West Indies, Mexico, and Central America. Now it is cultivated crop worldwide (Ross, 2007). Around 0.25% of India's cultivated land is used for tobacco production. Andhra Pradesh, Gujarat, Karnataka and Uttar Pradesh together account for over 90% of the total tobacco production in the country (Goyal et al., 2004). It is also grown in Bihar, Maharashtra, Orissa, Tamil Nadu, and West Bengal. The tobacco plant attracted the attention of several investigations. It accounts for millions of deaths each year from cancer, emphysema and heart disease. Yet, in certain neurologic and psychiatric conditions, nicotine can have useful therapeutic effects. For tribes throughout North America, the use of traditional tobacco plants for spiritual, ceremonial and medicinal purposes goes back thousands of years. Most indigenous nations have traditional stories explaining how tobacco was introduced to their communities, many of which emphasized the sacred properties of the plant, containing both the power to heal if used properly and the power to cause harm if used improperly (Binorkar and Jaini, 2012).

The tobacco plant is a coarse, large-leaved perennial, usually cultivated as an annual, grown from seed in cold frames or hotbeds and then transplanted to the field. Tobacco requires a warm climate and rich, well-drained soil. The plant is susceptible to numerous bacterial, fungal, and viral diseases (e.g., the tobacco mosaic virus) and is attacked by several species of worms, beetles, and moths. The characteristics of many of the named grades depend upon the regional environmental conditions and cultivation techniques. Tobacco leaves are picked as they mature, or they are harvested together with the stalk. Tobacco leaves are cured, fermented, and aged to develop aroma and reduce the harsh, rank odor and taste of fresh leaves.

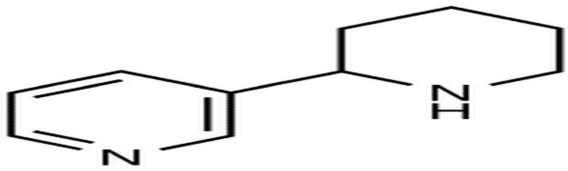
Fire-curing, dating from pre-Columbian times is done by drying the leaves in smoke; in air-curing, the leaves are hung in well-ventilated structures; in flue-curing, used for over half the total crop, the leaves are dried by radiant heat from flues or pipes connected to a furnace. The cured tobacco is graded, bunched, and stacked in piles called bulks or in closed containers for active fermentation and aging. Most commercial tobaccos are blends of several types, and flavorings e.g., maple and other sugars, are often added (Columbia Electronic Encyclopedia, 2012).

CHEMICAL CONSTITUENTS

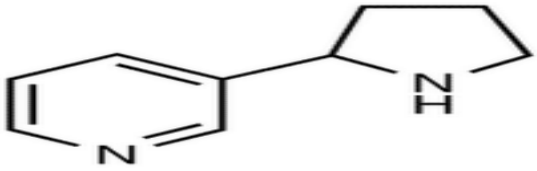
Tobacco leaf contains several pyridine alkaloids, the principal one being a liquid alkaloid, nicotine. Other alkaloids present include nicoteine, nicotimine, anabasine anatalline and nor-nicotine. It also contains a high percetntage of organic acids. Leaves also contain glucosides, tahacinin, tahacilin and *iso*-quercitrin, 1-quinic, chlorogenic, caffeic and oxalic acids. They also contain terpenic and carcinogenic substances (Shaligram and Nighantubhushanam, 2004). Anatabine and (+)nornicotine have been isolated from roots. Quercetin-3,3-dimethyl ether and quercetin-3-Me ether have been isolated from flowers. Three new gibberellins-nicotiana α, β and γ along with gibberllins A and A3 have been isolated from shoot apices and flower buds. Seed contains cycloartanol, cycloartenol 24-daturadiol and solavetivone. Cholesterol, cholest-7-enol, 24-methylenecholesterol, campesterol, stigmasterol, sitosterol, 28-isofucosterol, lanosterol, 31-norlanosterol, lanost-8-enol, obtusifoliol, 31-norcycloartenol, cycloeucalenol, granisterol, citrostadienol, β-amyrin, lupeol, cycloartanol and 24-methylenecycloartanol have also been reported in seed oil (Bapala and Adarsha, 2009). After leaves are smoked the nicotine decomposes into pyridine, furfurol, collidine, hydrocyanic acid, carbon monoxide, etc. The poisonous effects of tobacco smoke are due to these substances of decomposed nicotine. A protein of the white brown complex subfamily can be extracted from the leaves. It is an odorless, tasteless white powder and can be added to cereal grains, vegetables, soft drinks and other foods. It can be whipped like egg whites, liquefied or gelled and can take on the flavor and texture of a variety of foods. It is 99.5% protein, contains no salt, fat or cholesterol. It is currently being tested as a low calorie substitute for mayonnaise and whipped cream. The chemical structure of main constituent, nicotine, nicotinic acid and nor-nicotine:-



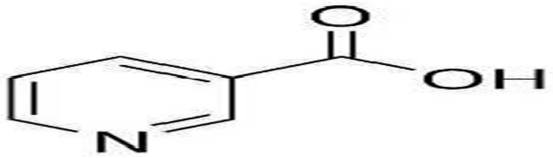
Nicotine



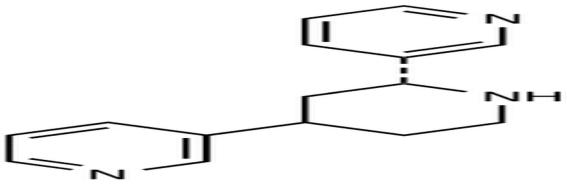
Anabasine



Nicotinic acid



Nor-nicotine



Anatalline

USES

The whole plant, leaves, flowers, seeds & roots, and individual chemical constituents, all are used as medicinally, traditionally & abused in entire world as a local irritant; if used as snuff it causes violent sneezing, with copious secretion of mucous; chewed, it increases the flow of saliva by irritating the mucous membrane of the mouth; injected into the rectum it acts as a cathartic. In large doses it produces nausea, vomiting, sweats and great muscular weakness. The alkaloid nicotine is a virulent poison, producing great disturbance in the digestive and circulatory systems. In the heart, causing palpitation and cardiac illness & vascular contraction, and is considered one of the causes of arterial degeneration. Nicotine acts like coniine and lobeline in its pharmacological action, and the pyridines in the smoke modify very slightly its action. Tobacco was once used as a relaxant, but is no longer employed except occasionally in chronic asthma. Its active principle i.e. nicotine is readily absorbed by the skin, and serious, even fatal, free application on the

surface of the skin has causes poisoning. The smoke acts on the brain, causing nausea, vomiting and drowsiness. Medicinally it is used as a sedative, diuretic, expectorant, discutient, & sialagogue, and internally only as an emetic, when all other emetics fail. The smoke injected into the rectum or the leaf rolled into a suppository has been beneficial in strangulated hernia, also for obstinate constipation, due to spasm of the bowels, also for retention of urine, spasmodic urethral stricture, hysterical convulsions, worms, and in spasms caused by lead, for croup, and inflammation of the peritoneum, to produce evacuation of the bowels, moderating reaction and dispelling tympanitis, and also in tetanus. To inject the smoke it should be blown into milk and injected, for croup and spasms of the rima glottides it is made into a plaster with Scotch snuff and lard and applied to throat and breast, and has proved very effectual. A cataplasm of the leaves may be used as an ointment for cutaneous diseases. The leaves in combination with the leaves of belladonna or stramonium make an excellent application for obstinate ulcers, painful tremors and spasmodic affections. A wet tobacco leaf applied to piles is a certain cure. The inspissated juice cures facial neuralgia if rubbed along the tracks of the affected nerve. The quantity of the injection must never exceed a scruple to begin with; half a drachm has been known to produce amaurosis and other eye affections, deafness, etc. Externally nicotine is an antiseptic. It is eliminated partly by the lungs, but chiefly in the urine, the secretion of which it increases. Formerly Tobacco in the form of an enema of the leaves was used to relax muscular spasms, to facilitate the reduction of dislocations. A pipe smoked after breakfast assists the action of the bowels. The pituri plant contains an alkaloid, pitarine, similar to nicotine, and the leaves are used in Australia instead of tobacco. An infusion of tobacco is generally used in horticulture as an insecticide (Grieve, 1995; Charlton, 2004).

(a) External uses

Tobacco use externally in case of bites of poisonous reptiles and insects; hysteria; pain, neuralgia; laryngeal spasm; gout; growth of hair; tetanus; ringworm; rodent ulcer; ulcers; wounds and as respiratory stimulant (Stewart, 1967).

(b) Medicinal uses

(i) Antibacterial activity

Nicotine, isolated from leaves of *Nicotiana tabacum* was complexed with zinc and studied for their antibacterial activities against ten different strains of Gram+ve and Gram-ve bacteria. Results showed that nicotine and zinc complex is more effective against different types of bacterial strains as compared to zinc metal salt used for complexation and nicotine alone (Zaidi et al., 2012).

(ii) Antifungal activity

Different isoforms of chitinases and 1,3-glucanases of tobacco were tested for their antifungal activities against *Fusarium solani* germlings, resulting in lysis of the hyphal tips and in growth inhibition. However, the extracellular washing fluid from leaves of transgenic plants expressing either of the secreted class-I enzymes exhibited antifungal activity on *Fusarium solani* germlings in vitro comparable to that of the purified vacuolar class-I proteins. Mixing extracellular washing fluid fractions from these plants revealed synergism in inhibitory activity against *Fusarium solani* (Anee et al., 1994).

(iii) Antimicrobial activity

The antimicrobial activity of extracts of twelve Nigerian medicinal plant species and a *Nicotiana tobacum* used in traditional medicine for the treatment of tuberculosis and cough were screened for activity against *Mycobacterium tuberculosis isolated* from tuberculosis patient sputum and the control strains of *M. tuberculosis*. Both ethanolic and aqueous solution of the extract of *Allium ascalonicum*, *Terminalia glaucescens*, *Allium cepa* and *Securidaca longepedunculata (*ethanolic extract only) at 0.05 g/ml as well as aqueous solution of wonder cure concoction at same concentration inhibited the growth of *M. tuberculosis*. Aqueous and ethanolic extract of *Nicotiana tobacum* used as medicinal plant extract in treatment of tuberculosis (Adeleye et al., 2008).

(iv) Anthelmintic activity

In-vitro and *in-vivo* anhelmintic activity of *Nicotiana tabacum Linne* leaves was studied to rationalize its traditional use. Live *Haemoncnus contortus* were used to assess the in-vitro anthelmintic effect of a crude aqueous extract and methanol extract, for the in-vivo studies both the extract were administered in increasing dosed (10-3.0g/kg) to sheep naturally infected with mixed species of gastrointestinal nematodes. The results of the study showed that both the extract possess dose-dependent anthelmintic activity. It Justify the use of plant in traditional system of medicine (Anita et al., 2008).

(v) Peripheral nervous system activity

The major action of nicotine consists initially of transient stimulation and subsequently of a more persistent depression of all autonomic ganglia. Nicotine also possesses a biphasic action on the adrenal medulla: small doses evoke the discharge of catecholamines, and larger doses prevent their release in response to splanchnic nerve stimulation. Nicotine, like acetylcholine

is known to stimulate a number of sensory receptors (Cheeta et al., 2000).

(vi) Central nervous system activity

The extract of nicotiana tabacum show different action on central nervous system. Nicotine is chief chemical compound which show several pharmacological activity. Nicotine markedly stimulates the CNS. Low doses produce weak analgesia; with higher doses tremors leading to convulsions at toxic doses are evident. The excitation of respiration is a prominent action of nicotine. Nicotine induces vomiting by both central and peripheral actions. The primary sites of action of nicotine in the CNS are pre-junctional, causing the release of other neurotransmitters. Accordingly, the stimulatory and pleasure-reward actions of nicotine appear to result from release of excitatory amino acids, dopamine, and other biogenic amines from various CNS centers (Francis et al., 1999).

(vii) Cardiovascular system activity

Plant extracts of *Nicotiana tabacum* show cardiovascular activity. The cardiovascular responses to nicotine are due to stimulation of sympathetic ganglia and the adrenal medulla, together with the discharge of catecholamines from sympathetic nerve endings. Also contributing to the sympathomimetic response to nicotine in the activation of chemoreceptors of the aortic and carotid bodies, these reflex results in vasoconstriction, tachycardia, and elevated blood pressure (Francis et al., 1999).

(viii) Gastrointestinal tract activity

Plant extract give different effect in gastrointestinal tract system. The combined activation of parasympathetic ganglia and cholinergic nerve endings by nicotine results in increased tone and motor activity of the bowel (Khalifa, 2001).

(ix) Exocrine glands activity

Plants extract show effect on exocrine glands. Nicotine itself exhibit effect on exocrine glands. Nicotine causes an initial stimulation of salivary and bronchial secretions that is followed by inhibition (Sairam et al., 2001).

(x) Hematological activity

The tobacco plant has been used for several years, irrespective of the location of human races. The aqueous extract of tobacco leaves was administered (11.7 and 5.8mg/kg, p.o.) for 26 days in rats. The results showed that the extract decreased significantly red blood cell count, packed cell volume, hemoglobin and platelet count and increased mean cell volume and mean cell hemoglobin. However, white blood cell count, percentage neutrophils, lymphocytes eosinophils were not significantly affected (Adeniyi and Ghazal, 2012).

(xi) Effect on body weight

The average body weight in each of the groups A, B and C were calculated on the day 1, 6, 11, 16, 21, and 27 of the experimental procedures. Using p-value=0.05, there was a significant decrease in the body weight between groups A and B compared to group C (Adeniyi and Ghazal, 2012). The observed retarded increase in body weight in groups A and B could be due to the negative effects of the extracts on the normal metabolism as reported by West and Russell (1985).

(xii) Anti-nociceptive activity

The anti-nociceptive activities of the methanolic leaf extract of *Nicotiana tabacum* was evaluated using tail immersion, hot plate and acetic acid- induced abdominal constrictions or writhing in mice (Trease and Evans, 1996). Doses of 100, 200 and 300mg/kg body weight of the extract were used orally while indomethacin (10mg/kg body weight) was used as standard drug. In the tail immersion and hot plate test, *Nicotiana tabacum* exhibited good level of anti-nociceptive activities by significantly increasing the pain reaction time or latency period in the mice in a dose dependent manner (Harboume, 1991). In the acetic acid-induced writhing test *Nicotiana tabacum* and indomethacin, significantly decreased the mean total number of abdominal constrictions or writhes in a dose dependent manner and also the percentage protection of the abdominal constriction reflex was increased from zero percent in the negative control group, at the dose of 300mg/kg of the extract. Methanolic leaf extract of *Nicotiana tabacum* showed significant anti-nociceptive activity and may be acting through both central and peripheral nociceptive mechanisms (Maxwell and Omeh, 2010).

(xiii) Anti-Alzheimer's activity

Memory is the ability of an individual to record the information and recall it whenever needed. Dementia is a mental disorder characterized by loss of intellectual ability (judgment or abstract thinking) which invariably involves impairment of memory. The most common cause of dementia is Alzheimer's disease, which is a progressive neurodegenerative disorder associated with loss of neurons in distinct brain areas and cord. Nicotiana tabacum plants extract show anti-Alzheimer's activity and improved memory (Scerri, 2005).

(c) Traditional uses

In *Ayurveda* texts tobacco is referred as *Tamakhu, Ksharapatra, Krimighni, Dhumrapatrik* (Shaligram and Nighantubhushanam, 2004), *Vajrabhringi* (Bapala and Adarsha, 2009), *Bahubeeja*, Bahuphala, *Sukshmabeeja*, *Deerghaka* (Shastry and Vidyotini, 1999). The *Ayurvedic* pharmacology indicates that it is *Ushna* (hot), *Tikshna* (Sharp), *Sara* (stimulates peristaltic movements) and increases Pitta *(*Digestive fire/bile juice/enzymatic

metabolisms). It is a drug of choice in *Bastivishodhana* (Urinary track disorders and diseases related with urinary bladder). It is bitter and pungent in taste. In proper dosing it can be used in *Kapha* (cough), *Shwasha* (Asthma), *Kandu* (itching), *Krimi* (anti-helminthes). It is very good as analgesic and utilized in *Dantaruja* (dental pain), *Shukraruja* (pain related with genital organ) and *Drishtiruja* (pain related with eye). It can control dandruff and hair infections. It can dwindle the poison of scorpion bite and related swelling (Shastry and Vidyotini, 1999). The clever administration of the drug effective in *Madakrit* (narcotic), *Bhramaka* (Induces vertigo), *Drishtimandyakara* (diminishes the vision) and Vamaka (Emetic). Tobacco has been used as antispasmodic, irritants, discutients, diuretic, emetic, expectorant, sedative, sialagogue and in homeopathy. Tobacco has a long history of use by medical herbalists as a relaxant, though since it is a highly addictive drug it is seldom employed internally or externally at present. Wet tobacco leaves are applied externally in the treatment of rheumatic swelling, skin diseases and stings, as the active ingredients can be absorbed through the skin. They are also a certain cure for painful piles. A homeopathic remedy made from the dried leaves is used in the treatment of nausea and motion sickness. Some other activities reported for *Nicotiana tabacum* are: analgesic activity, anesthetic activity, angiogenesis inhibition, antibacterial activity, anti-convulsant activities, anti-estrogenic effect, antifungal activity, anti-glaucoma activity, antioxidant activity, anti-stress effect, antiviral activity, aromatase inhibition, arrhythmogenic effect, carcinogenic activity, Nicotine for treatment of Alzheimer disease, Parkinson disease, depression and anxiety, schizophrenia, attention deficit hyperactivity disorder, pain, and obesity (Binorkar and Jani, 2012). The countries that have histories of use of the plant include:-

Argentina: Leaves are smoked by adults during healing rituals (Desmarchelier, 1996). If baby suffers stomach problems, then aromatic herbs together with black wool, tobacco and chuspa-e-cacu (the nest of *Cacicus chrysopterus*; Icteridae, Aves) should be fumigated around his craddle and his anus (Martinez and Lujan, 2011). Tobacco is used to treat distemper in veterinary with milk and cooking oil, Lemon, onion and milled tobacco with white soap in warm water are used to treat scabies in animals (Hirschmann and De-Arias, 1990). It is applied in snake bites with milk & oil, or fried in oil and *Tanacetum parthenium* (Martinez and Lujan, 2011).

Brazil: Dried leaves are used as an insecticide (Bhattarai, 1992) & rub a decoction of the leaves over sprains and bruises. The leaf juice is taken orally to induce vomiting & narcosis. It is also reported that the herb used for ulcerated abscesses, fistulas, sores, inveterate polyps and many other ailments (Bhattarai, 1992; Barrett, 1994).

China: The traditional use of *Apocynum venetum* with tobacco as an agent to detoxify nicotine (Xie et al., 2012).

Colombia: Poultice prepared from fresh leaves is used over boils & infected wounds. Crushed leaves with oil from palms used to prevent baldness (Schultes, 1995).

Cuba: The leaf extract is taken orally for the treatment of dysmenorrhea (Roig and Mesa, 1945).

East Africa: Dried leaves of *Nicotiana tabacum* and Securinega virosa are mixed into a paste and used externally to destroy worms in sores (Hedberg, 1983).

Ecuador: The leaf juice is used for indisposition, chills, and snake bite and in the treatment of pulmonary disorders (Schultes, 1995).

Egypt: Dried leaves & flowers are smoked to relieve asthma and influenza. Leaves are used as a poultice with oil in rheumatic pain (Hedberg, 1983).

Fiji: Fresh root is taken orally for Asthma and indigestion. Fresh root juice is applied opthalmically as a drop for bloodshot eyes. Seeds are taken orally for rheumatism and to treat hoarseness (Singh, 1986).

Guatemala: Leaves are applied externally for myosis, headache and wounds (Giron et al., 1991). Hot water extract of dried leaf are applied externally for ringworms (Caceres et al., 1991), ulcers, bruises sores & stomatitis (Caceres et al., 1987a). The leaf is taken orally for kidney diseases (Caceres et al., 1987b). A mixture of leaf with menthol is applied externally in children for cough (Comerford, 1996).

Haiti: Decoction of dried leaf is taken orally for bronchitis and pneumonia (Weniger, 1986; Bhattarai, 1992).

India: Juice of *Securinega leucopyrus* is mixed with the dried leaves of *Nicotiana tabacum* and applied externally for parasites (Nagraju and Rao, 1990); Fresh leaves are mixed with corncob or *amorphophallus paeonifolium* to treat asthma (Singh, 1996). The leaves of the tobacco plant have been used in traditional medicine as a sedative, antispasmodic, and vermifuge. They are also considered as antiseptic, emetic and narcotic. A decoction of leaves is applied locally for muscle relaxation associated with joint dislocation. It is also used to relieve pain and swelling associated with rheumatic problems. Tobacco is also utilized traditionally to treat strangulated hernia, orchitis and skin diseases. The tribal inhabitants of Surguna district of Madhya Pradesh apply warmed leaves on testis to treat hydrocele. Even the oil extracted from the leaves is used in the treatment of arthralgia, gout and lumbago

(Zaidi et al., 2012). Tobacco powde & masheri, is rubbed on the teeth and tobacco toothpaste is also available (Anee et al., 1994).

Iran: Ointments made from crushed leaves are used for baldness, dermatitis, infectious ulcers and pediculicide (Bhattarai, 1992). Juice is applied externally as an insect repellent (Zargari, 1992). Leaf is added to betel quid and used as a mild stimulant (Vanio, 1986).

Kenya: Water extracts of tobacco are applied opthalmically for corneal opacities and conjunctivitis (Loewenthal and Peer, 1991).

Malaysia: Infusion of the dried leaf of tobacco is administered orally as a sedative (Ilham, 1995).

Mexico: Extract of the plant with saliva massaged on the abdomen to facilitate expulsion of placenta (Viesca-Trevino, 1976). Exudates from stem and leaf are used in cases of gum inflammation (Flores, 1996). It is also used as an anti-diarrheal, narcotic and emollient. Tobacco leaves were applied for the relief of pain, in powdered form for the relief of catarrh and applied locally to heal wounds and burns (Dickson, 1954). Fresh green leaves are ground with slaked lime to produce an intoxicating oral snuff that serves as both a protective and therapeutic agent (Groark, 2010).

Nepal: Tobacco Leaf juice is applied externally to treat scabies (Barrett, 1994)

Nicaragua: Leaves are chewed for tooth ache (Barrett, 1994). It is also applied externally for pain, stings and skin rashes (Coee, 1996).

Nigeria: Hot water extract of the fresh leaf is taken orally as a sedative (Adesina, 1982). The sun dried leaves are ground to smooth powder and used as a snuff or put on the tongue as a stimulant. For the treatment of convulsions, the leaf juice is used as a bath in water (Bhat et al., 1985).

Papua New Guinea: Dried plant mixed with the bark of Gaibulima *belgraveana* & *Zingiber officinale* is taken orally for head lice (Holdsworth and Sakulas, 1987). Tender leaf is chewed to relieve stomachache. Decoction of tender leaf is taken orally to treat gonorrhea (Holdsworth and Balun, 1992).

Paraguay: Extract of the plant is administered orally to cows as an insecticide and insect repellent (Schmeda-Hirschmann and De-Arias, 1992). Dried resin accumulated in stem of a smoking pipe is applied externally against botfly larvae and severe pediculosis (Arenas, 1987).

Peru: Decoction of the leaf with beverage is taken orally for hallucinating effect during shamanic training (Luna, 1984). Hot water extract of dried flower & leaf are used externally for snake & spiders bite (Ramirez, 1988). A curing ceremony normally involves purification of the patient by orally spraying blessed and enchanted herbal extracts on the whole body to fend off evil spirits and by nasal ingestion of tobacco juice and perfumes (Bussmann and Sharon, 2006). The fresh leaves as poultice used over boils & infected wounds. The mixed & crushed leaves with oils from palms as a hair dressing to prevent hair loss. The tobacco juice is use for indisposition, cold chills, and snake bite and to treat pulmonary ailments (Schultes, 1995).

Sierra Leone: Leaf is chewed and rubbed on area to dress umbilical stump.

Spain: Spanish missionaries recorded that breathing the odor of the fresh green leaves of the plant relieved persistent headaches, and that rubbing the leaves around the inside of the mouth relieved symptoms of colds and catarrh. Crushed, steamed tobacco leaves mixed with salt were used to treat swollen glands, by applying them directly over the affected area (Brookers, 1952).

Tanzania: Leaves of *Nicotiana tabacum* are placed in the vagina to stimulate labor (Moller, 1961).

Turkey: Powdered leaf is applied externally for wounds (Tabata, 1994).

United States: Extract of *Nicotiana tabacum* is taken orally to treat tiredness, ward off diseases, and quiet fear (Hussey, 1974). Tobacco, probably mixed with lime or chalk, appears to have been used as toothpaste to whiten the teeth (Brookers, 1937).

(d) Miscellaneous uses

All parts of the plant contain nicotine, which can be extracted and used as an insecticide. The juice of the leaves can be rubbed on the body as an insect repellent. The leaves can be dried and chewed as an intoxicant. The dried leaves remain effective for 6 months after drying and used as snuff or are smoked. *Nicotiana tabacum* is the main species that is used to make cigarettes, cigars, and other smokable tobacco preparations. A drying oil is obtained from the seed. Medicinally it is used as a sedative, diuretic, expectorant and internally as an emetic, when all other emetics fail. The sedative effect is produced by nicotine; whereas decoction of dried leaf can act as strong diuretic. Leaves may be used as an ointment for cutaneous diseases. The leaves in combination with the leaves of belladonna or stramonium make an excellent application for obstinate ulcers, painful tremors and spasmodic affections. Tobacco leaf applied to piles is a certain cure. The juice cures facial neuralgia if rubbed along the tracks of the affected nerve.

TOBACCO PRODUCTS

Tobacco products, including cigarettes, cigars, chewing tobacco, snuff, and loose pipe tobacco, contain the dried, processed leaves of the tobacco plant nicotiana tabacum or nicotiana rustica. All forms of tobacco

contain nicotine, an extremely addictive drug that can act as both a central nervous system stimulant and depressant. In addition to nicotine, tobacco contains thousands of other chemicals and additives to enhance the effects and flavor of the tobacco. Many of these chemicals are known to cause cancer and various other diseases.

Tobacco is most often smoked, usually in the form of cigarettes, cigars, or in pipes. Another method of smoking, usually found in India and the Middle East, is through a large water pipe, usually called a hookah, nargile (nar-gee-leh), or shisha. These types of pipes are commonly used to smoke flavored tobacco that includes pieces of fruit and is held together with sticky molasses. Other forms of smoking tobacco include bidis (bee-dees) - tobacco wrapped in a leaf and tied with a string-and clove cigarettes, which are basically normal cigarettes but include cloves for flavoring, or just cloves alone. Chewing tobacco or dip is a form of smokeless tobacco, in which the user holds the tobacco in his/her mouth, absorbing nicotine thorough the gums and tongue. Snuff is tobacco that has been dried and processed into a powder. This powder is snorted into the nose, where it is absorbed through the nasal passages.

HAZARDS OF TOBACCO USE

Tobacco has a potent effect on the brain, regardless of the route of administration. When a smoker inhales tobacco smoke, over 4,000 chemicals are released, including nicotine and hundreds of other carcinogens. Nicotine, when smoked, reaches the brain in a matter of seconds. Nicotine from chewing tobacco takes a little longer to reach the brain, as it must first be absorbed into the bloodstream through the gums. At any rate, when nicotine reaches the brain, it acts as a stimulant, causing the brain to release excess neurotransmitters including dopamine-a neurotransmitter associated with pleasure and motivation. A person can become addicted to nicotine even after just a few uses because the brain adjusts itself and develops a level of nicotine tolerance that the addict must reach in order to maintain the feeling of comfort. Once this comfort level has been established, a lack of nicotine in the brain will cause uncomfortable withdrawal symptoms. These withdrawal symptoms can make the user edgy and irritable, and using tobacco while in this state will have a sedative effect. It is important to note that smoking, whether it is called social smoking or simply trying a cigarette, can easily lead to an addiction (Sivnandam, 2010).

(a) Short-term effects of smoking or chewing tobacco

- Excess saliva production & drooling
- Bad breath; bad taste in mouth
- Sores, patches, and lumps in mouth or neck
- Difficulty in chewing, swallowing, & moving tongue or jaw
- Receding gums; permanent gum loss
- Stained & sensitive teeth or tooth decay
- Stains on clothing
- Smelly hair and clothes
- Damage to the respiratory system
- Decreased lung capacity, coughing, bronchitis & asthma
- Addiction to nicotine
- Increased likelihood of drug use and risky behavior
- Death from fire

(b) Long-term effects of smoking or chewing tobacco (Sivanandam, 2010)

Long-term tobacco use brings very serious health risks. About 181,000 people die each year in the United States from smoking-related heart disease and stroke, 158,000 die from smoking-related cancer, and about 123,000 die from other lung diseases.

(i) Cardiac complications

Tobacco use has many adverse effects on the heart, including hypertension, blocked blood vessels, weakened pumping of the heart, narrow arteries leading to heart attack and death. In addition, weakened blood flow to the brain can cause strokes.

(ii) Lung disorders

Smoking causes chronic bronchitis, changing the size and shape of the airways of the lungs, enlarging the mucous glands, and causing coughing and production of excess phlegm. It is also the leading cause of emphysema, a lung condition marked by an abnormal increase in the size of the air spaces, resulting in labored breathing and an increased susceptibility to infection (Sivnandam, 2010).

(iii) Thrombosis

Acute rupture or erosion of a coronary athermanous plaque and subsequent coronary artery may induced thrombosis. It causes the majority of sudden cardiac deaths and myocardial infarctions. Cigarette smoking is a major risk factor for acute coronary thrombosis. Indeed, a majority of sudden cardiac deaths attributable to acute thrombosis are in cigarette smokers. Both active and passive cigarette smoke exposure seem to increase the risk of coronary thrombosis and myocardial infarctions. Cigarette smoke exposure seems to alter the hemostatic process via multiple mechanisms, which include alteration of the function of endothelial cells, platelets, fibrinogen, and coagulation factors. This creates an imbalance of antithrombotic/prothrombotic factors and profibrinolytic/anti-fibrinolytic factors that support the initiation and propagation of thrombosis (Barua and Ambrose, 2013).

(iv) Anti-fertility

Tobacco use can cause reproductive damage, including abnormal sperm cells and impotence in men and menstrual disorders, early menopause, and difficulty maintaining pregnancy in women. The aqueous extract of *nicotiana tabacum* at doses of 20mg/kg and 30mg/kg when administered for a period of 21 days showed a significant decrease in sperm motility & concentration as well as decreased spermatogenic cells in the histology of the testis (Gambo et al., 2013).

(v) Cancer

Lung, upper respiratory tract, and cervical cancers are primarily found in smokers while stomach cancer is mainly found in chewing tobacco users. Other cancers that can attack users of both forms of tobacco include cancers of the larynx, mouth, throat, pancreas, kidney, and bladder (Sivanandam, 2010).

(vi) Other health complications

Smoking during pregnancy can lead to miscarriage, stillbirth, low birth weight, premature birth, or sudden infant death syndrome. Children born to women who smoked during pregnancy can develop upper respiratory problems, ear complications, asthma, and learning and behavior problems. Other damage that long-term tobacco use can cause includes prematurely wrinkled skin, gum and tooth loss, lost or weakened sense of taste and smell, weakened immune system, stomach ulcers, and unwanted weight fluctuation (Sivanandam, 2010).

NICOTINE-A BASE CONSTITUENT

Nicotine is an alkaloid organic compound, found naturally throughout the tobacco plant, with a high concentration in the leaves. It constitutes 0.3 to 5% of the plant by dry weight. The biosynthesis takes place in the roots and it is accumulated in the leaves. It is a potent nerve poison and is included in many insecticides. In low concentrations, the substance is a stimulant and is one of the main factors leading to the pleasure and habit-forming qualities of tobacco smoking. In addition to the tobacco plant, nicotine is also found in lower quantities in other members of the Solanaceae family, which includes tomato, potato, eggplant, and green pepper. Nicotine also found in the leaves of the coca plant. It has mild cocaine like effect on brain. It raises blood pressure and pulse rate by stimulating autonomic nervous system. *Pharmacological actions:* nicotine produces tachycardia and rise in blood pressure. It enhanced gut motility, in small dose it stimulate ganglionic cells but in large doses cause paralysis. It stimulates the release of adrenaline and ADH. It initially stimulates CNS followed by depression. Nicotine induces spasm followed by paralysis. It induce metabolic enzymes in liver and GIT. Initially stimulates respiration followed by depression. *Mechanism of action:* Initially stimulation and followed by depression of cholinergic receptors located on autonomic ganglia and skeletal muscles. *ADME:* Inhaled through cigarette smoke, easily penetrate mucus membranes and intact skin, metabolized in liver, lungs and excreted in milk and urine. *Interactions:* Potentiate effect of CNS depressants drugs. *Contra-indicated in:* Health concern because consumption of tobacco in any form injurious to health and precipitate cardiovascular diseases. *Dose:* Nicotine patches of 10, 20, 30 cm2, releasing 7, 14, 21 mg nicotine/24 hours. *Adverse effects due to poisoning:* Abnormal hunger, amblyopia, angina pectoris, anxiety, atherosclerosis, bronchial carcinoma, cardiac arrhythmias, change blood pressure, chest pain, chronic bronchitis, cold and influenza like symptoms, cold sweat, diarrhea, dizziness, dysmenorrhea, dyspepsia, gastric ulcer, headache, hiccups, high pulse rate, impaired concentration, incoordination, indigestion, insomnia, lung cancer, myalgia, myocardial infarction, myocarditis, nasal irritation, nausea, neuritis, nose bleeding, palpitation, psychological and physical dependence, rapid respiration, rashes, respiratory paralysis, salivation, somnolence, vivid dreams, vomiting, and watery eyes. *Uses:* No therapeutically used. It is use as insecticide, as experimental tools and to prevent cigarette smoking (Maheshwari, 2012).

It is a muscle relaxant, directly acts on nicotinic receptors in the peripheral nervous system. It binds to the nicotinic receptors at the junction between the nerve and muscle and causes muscle relaxation. It is particularly useful in assisting the reduction of fractures and dislocations. The muscular spasms oppose efforts to adjust the position of the bone and contribute to the pain. The administration of an analgesic and a muscle relaxant are useful. Allowing a smoker to have a cigarette may help but in severe cases general anesthetic is usually required. A cigar is inserted into the rectum leaving at least a third of its length outside. The tobacco is removed from 5-10 cigarettes and placed into a cloth bag, which is then inserted into the rectum via anus so that an end which can be easily grasped remains outside. Sterile water is used as a lubricant, and, if a bag is used, the contents should also be thoroughly moistened prior to being inserted. After 5-15 min, the muscles should relax sufficiently to allow a successful reduction. It can be used to control some intestinal parasites and worms. It is also an effective insecticide and can be spray on vegetables to prevent insect infestations.

(i) Effects of nicotine on body

In cigarette smoke, over 4,800 different chemical compounds have been identified. Most of them produce serious hazards on human health, and more than 60 of

them are recognized as carcinogenic. The nicotine is a minor stimulant of the brain. Like other psychoactive substances nicotine cause dependence, it makes certain nerve cells in the brain to secrete more dopamine. Nicotine also imitates the effects of acetylcholine, by binding to the same receptors in the brain. In addition, nicotine facilitates the release of endorphins, which would partly explain its analgesic effect. In small doses nicotine has a stimulating effect, increasing activity, alertness and memory. Repeat users report a pleasant relaxing effect. It also increases the heart rate and blood pressure and reduces the appetite. In large doses it may cause vomiting and nausea. Repeat users of nicotine often develop a physical dependency to the chemical. Withdrawal symptoms include irritability, headaches and anxiety. These symptoms may last for months or years, although they peak at around 48-72 hours.

As nicotine enters the body, it quickly gets distributed & can cross the blood-brain barrier and within seven seconds reach the brain. It acts on nicotine receptors and even in small dose it increases the activity of these receptors. With other things nicotine leading to an increased flow of adrenaline. The release of adrenaline causes an increase in heart rate, blood pressure and respiration, as well as higher glucose levels in the blood. Cotinine, a metabolic product of nicotine which remains in the blood for up to 48 hours, and so can be used as an indicator of a person's exposure to smoke. In high doses, nicotine blocks the nicotinic acetylcholine receptor, which is the reason for its toxicity and its effectiveness as an insecticide. In addition, nicotine increases dopamine levels in the reward circuits of the brain. Studies have shown that smoking tobacco inhibits MAO, an enzyme responsible for breaking down monoamines such as dopamine, in the brain. Thus nicotine generates feelings of pleasure as similar as cocaine and heroin, and is another reason people keep smoking: to sustain high dopamine levels. It has been noted that the majority of people diagnosed with schizophrenia smoke tobacco (Jahn, 2002; The Columbia encyclopedia, 2008).

(ii) Effects on diseases

Nicotine and its metabolites are being evaluated for the treatment of various disorders, including ADHD, Parkinson's disease and Alzheimer's disease. It has long been thought that tar and other chemicals in tobacco were the main cause of cancer but recent studies showed that nicotine alone has carcinogenic properties by inhibiting the natural ability of the body to get rid of cells with significant genetic damage before they turn cancerous.

(iii) Nicotine poisoning

The onset of symptoms in acute nicotine alkaloid poisoning is usually rapid. In the case of ingestion of leaves and other parts of the plant there is a delay in the onset of the symptoms due to slower gastric absorption of the alkaloid. Symptoms following a relatively small dose are transient and consist of salivation, nausea, vomiting, diarrhea, bradycardia and dizziness. In severe poisoning with pure alkaloid, the patient may collapse and die within minutes from overwhelming paralysis. Where death is delayed, abdominal pain is marked with severe diarrhea and a cold sweat. Mental confusion, giddiness, restlessness, muscular weakness and disturbed vision and hearing are followed by a loss of coordination, and unconsciousness. Blood pressure may initially be raised and respiration stimulated, but is soon followed by a fall in blood pressure, a rapid irregular pulse and labored breathing. Clonic convulsions are followed by collapse and complete muscle relaxation. Reflexes disappear and respiration becomes slow and weak, followed by respiratory arrest.

In cases of nicotine poisoning, the stomach should be quickly emptied, and repeated doses of tannic acid given, the person kept very warm in bed, and stimulants such as caffeine, strychnine, or atropine given, or if there are signs of respiratory failure, oxygen must be given at once (Landoni, 1990).

CESSATION OF SMOKING

Nicotine is one of the most addictive substances known to humankind. In the face of grossly negative consequences, many people are still unable to quit the habit. Today there are many treatments available for someone trying to kick the habit. Nicotine replacement treatments such as nicotine gum and patches can help relieve cravings, and recently nicotine nasal sprays, inhalers, and mints have been introduced. Also, the antidepressant bupropion has been shown to be an effective treatment for limiting tobacco cravings (Sivanandam, 2010). There are also behavioral treatments that can help train a person to avoid smoking. In general, develop self-monitoring of smoking behavior, and establish coping responses. The following agents can also help to reduce smoking. (i) Nicotine replacement agents-Nicotine gum, Nicotine patches, Nicotine inhaler and Nicotine nasal spray (Balfour and Fagerstrom, 1996). (ii) Other agents-Bupropion, Cotinine, Mecamylamine+nicotine and Methoxsalen+nicotine.

TOBACCO AND ANTIOXIDANT

The commercial tobacco products have moderate-to-high antioxidant properties, much like fruits and vegetables. The journal of tobacco science reports that antioxidants may have demonstrable local and systemic health effects that are positive, especially for smokeless tobacco users. The human body constantly produces potentially damaging molecules known as reactive

oxygen species or free radicals. These are countered by antioxidant agents, which the body generates and are also available in fruits & vegetables. Eating antioxidant-rich foods has been shown to reduce mortality from cardiovascular disease and cancer (Lip and Hart, 2002). Tobacco contains significant concentrations of polyphenols and carotenoids, which are important naturally occurring antioxidants. Cigarette smoking, however, is associated with low plasma antioxidant levels, which may result from the large numbers of free radicals that are created when tobacco is burned. In contrast, plasma antioxidant levels in users of smokeless tobacco are similar to those of nonusers of tobacco. High antioxidant levels in smokeless products may explain why even long-term users have only a low risk for mouth cancer. Carotenoids have been shown to inhibit formation of cancerous lesions and produce clinical regression of white patches called keratosis. Polyphenols, which are responsible for most of the antioxidant activity in fruits and vegetables, also inhibit the formation of tumors in experimental systems. Smokeless tobacco, in the form of chewing tobacco or moist snuff, has been shown to involve only two percent of the health risks of smoking. In fact, recent epidemiologic studies have shown little or no mouth cancer risk. Dr. Rodu and Ou (2004) measured the antioxidant activity of 16 smokeless and cigarette products. Those included 10 moist snuff products, two chewing tobacco products, two pelletized leaf tobacco products, and two cigarette brands. They employed the oxygen radical absorbance capacity (ORAC) assay, which measures inhibition of damage by the peroxide radical, one of the most common ROS in-vivo. The ORAC assay has been used to measure the antioxidant capacity of a wide range of biological samples, from pure compounds to fruits, vegetables and animal tissues. The 16 tobacco products had a range of antioxidant activity from modest to high and there was a strong correlation between ORAC level and total beneficial phenolic content. The range of ORAC activity in the tobacco products was similar to that reported for many fruits and vegetables. Tobacco is a vegetable. Smoking it, however, causes carcinogens and dangerous gases to be formed, making the antioxidant benefits to be canceled out. However, smokeless tobacco users do not inhale the byproducts of combustion, which makes the antioxidant effects more pronounced (Roud, and Ou, 2004).

TOBACCO AND THROMBOSIS

It is widely held that smoking is a causative factor in Buerger's disease and there is evidence that there is an increased incidence of coronary artery disease among smokers. The constituents of tobacco and particularly nicotine have widespread effects notably on the dynamics of the circulation. It is true that thrombus formation in flowing blood in an extracorporeal circulation is little affected by rate of blood flow over quite a wide range (Rowsell et al., 1966) but this might not be true inside the body and especially in the smaller blood vessels. Grassi and Caltabiano (1956) developed a general conclusion that blood coagulation is promoted by smoking. Eisen (1958) studied on four patients who were habitual smokers but who had abstained for at least one month. They then smoked three to four, cigarettes in rapid succession. Lee-White clotting times were done before and after smoking. The results shown that after smoking the clotting time get reduced. Horwitz and Waidorf (1960) studied on ten patients, five male and five female, 21-44 years of age, before and after smoking a cigarette, a control group which did not smoke. Blood coagulation was studied by thromboelastography which measures the speed and quality of clot formation. They interpret this to mean that the strength of the clot was enhanced. On the other hand, using citrated blood, found that nicotine added in-vitro produces considerable delay in clotting, and with high doses, inhibition for days. Wenzel et al., (1960; 1961; 1962) found that intravenous or oral administration of nicotine in rabbits shortens coagulation time both acutely and over a long period. Blood coagulation was assessed by capillary clotting time. The effect was somewhat enhanced if extra cholesterol in cotton seed oil was given by mouth. There is good evidence that nicotine acts, at least in part, by releasing endogenous epinephrine. Kershbaum et al., (1963) found that smoking increased the amount of free and total catecholamines in three-hour collections of urine and raises the free fatty acid level in the blood.

There is evidence that smokers have higher blood cholesterol levels than nonsmokers (Karvonen et al., 1959; Thoma, 1960). Thus the relationship between blood cholesterol and smoking in population studies may not in any way indicate direct causality. The relevance of cholesterol to thrombosis and coagulation is uncertain, but it may seriously interfere with the ease with which scavenging processes such as fibrinolysins and other mechanisms dispose of thrombi (Ban and Cliffton, 1960).

DISCUSSION

India has an ancient heritage of traditional medicine. The materia medica of India provides a great deal of information on the Ayurveda, folklore practices and traditional aspects of therapeutically important natural products. Tobacco is a plant with an extraordinary history of use. It commenced with a history of sacred

worship in the Native American Pipe ritual, when smoking tobacco would support and clear the mind as the smoke was believed to carry one's prayers to the Great Spirit. In addition, it had a wide variety of uses for physical complaints, such as venomous bites and stings, internal and external parasites, and the symptomatic relief of pain, which justifies its wide use and appreciation by traditional practitioners all over the world (Haber, 1994). Even though Tobacco has long been removed from pharmacopoeias and from medical practice historically, tobacco has been an essential element in the ceremonial aspects of many communities and has taken on many sacred roles throughout the culture. Tobacco was, and is, a sacred plant used for spiritual, emotional, mental and physical guidance. The smoking and chewing products derived from this plant, few people realize its many other uses. It has medicinal values, makes an extremely valuable ornamental plant and flower garden specimen and is used to make one of nature's finest biodegradable, all natural pesticides (Nan-Ren and Michael, 2001). Many Ayurveda philosophers and healers praised about the properties of this plant and utilized in various disorders. Although tobacco is still used traditionally in its historic manner by many tribes and by many native people, the continued abuse of the commercial tobacco is much more frequent and has taken its toll on the native people's health. Poisoning has been reported from percutaneous absorption in tobacco harvesters, during manufacture and the workers in the tobacco industry (Landoni, 1990). The drug, Nicotiana is also capable of producing dependency in chronic users. That's why there is an incredible amount of difficulty in explaining how this sacred and powerful gift has been shape-shifted and became the cause of such deadly consequences. One must keep in mind regarding the dosage of administration particularly if it's being used orally and secondly, the duration of such oral administration should be supervised to avoid dependency and abusive usage of the tobacco when it is intended for medicinal purpose.

CONCLUSION

Tobacco causes addiction and dependence but it has many practical folklore traditional medicinal uses (Sairam et al., 2001). If it is used in positive ways it had the power to heal and protect; but if misused, it had the power to harm (Giannopoulou et al., 2003). It possesses various pharmacological activities (Greer and Poulson, 1983). The ethnomedical uses include the use of the decoction of leaves as antispasmodics, diuretics, emetics, expectorants, sedatives, and in rheumatic swellings, anesthetics, antibacterial, antimicrobial, anthelmintic, anticonvulsants and for anti-fungal activities. Tobacco also use for the treatment of asthma by Indians, treatment of worms in East Africa, treatment of wounds in Columbia and treatment of dysmenorrheal in Cuba among others. The plant *Nicotiana tabacum* have great activities on peripheral nervous system, central nervous system, cardiovascular system, gastrointestinal tract, exocrine glands, Haematopoietic system, algesia, Alzheimers and on body weight. The plant also have great traditional value worldwide as it used as *Ushna* (hot), *Tikshna* (Sharp), *Sara* (stimulates peristaltic movements) and increases Pitta *(*Digestive fire/bile juice/enzymatic metabolisms). It is a drug of choice in *Bastivishodhana* (Urinary track disorders and diseases related with urinary bladder). In proper dosing it can be used in *Kapha* (cough), *Shwasha* (Asthma), *Kandu* (itching), *Krimi* (anti-helminthes). It is very good as analgesic and utilized in *Dantaruja* (dental pain), *Shukraruja* (pain related with genital organ) and *Drishtiruja* (pain related with eye). It can control dandruff and hair infections. It can dwindle the poison of scorpion bite and related swelling (Shastry and Vidyotini, 1999). The drug effective in *Madakrit* (narcotic), *Bhramaka* (Induces vertigo), *Drishtimandyakara* (diminishes the vision) and Vamaka (emetic). Tobacco has been used as antispasmodic, irritants, discutients, diuretic, emetic, expectorant, sedative, sialagogue and in homeopathy. Tobacco has a long history of use by medical herbalists as a relaxant. Since tobacco causes addiction and dependence, it is seldom used internally or externally now-a-days. Wet tobacco leaves are applied externally in the treatment of rheumatic swelling, skin diseases, stings and cure for painful piles. A homeopathic remedy made from the dried leaves is used in the treatment of nausea and motion sickness. Some other activities reported for *Nicotiana tabacum* are: analgesic activity, anesthetic activity, angiogenesis inhibition, antibacterial activity, anti-convulsant activities, anti-estrogenic effect, antifungal activity, anti-glaucoma activity, antioxidant activity, anti-stress effect, antiviral activity, aromatase inhibition, arrhythmogenic effect, carcinogenic activity (The biggest plant dictionary, 2011), Nicotine for treatment of Alzheimer disease, Parkinson disease, depression and anxiety, schizophrenia, attention deficit hyperactivity disorder, pain, and obesity (Binorkar and Jani, 2012). Therefore, some potential activities which are still unexplored on the various parts of the plant may be evaluated (Rawat and Mali, 2013).

REFERENCES

1. Adeleye, A., Conubogu, C. and Ayolabi, C.I. (2008). Screening of crude extracts of twelve medicinal plants and wonder cure concoction used in Nigeria unorthodox medicine for activity against *mycobacterium tuberculosis* from tuberculosis patients sputum. African J. Biotichnol., 7(18), 3182-3187.
2. Adeniyi, P.A.O. and Ghazal, O.K. (2012). Effects of Tobacco (Nicotiana Tabacum) Leave Aqueous Extract on Haematological Parameters in Wistar Rats. University of Ilorin, Nigeria, Publication.
3. Adesina, S.K. (1982). Studies on some plants used as anticonvulsants in Amerindian & African traditional medicine. Fitoterapia, 53,147-162.
4. Akehurst, B.C. (1968). Tobacco, Longmans, Green and Co., London. 2-11.
5. Anee, S., Sandra, P., Vloemans, A.B., Marianne, B. and Buurlage, S. (1994). A novel pathogen- and wound-inducible tobacco (NIcotiana tabacum) protein with antifungal activity. Plant Physiol., 104, 109-118.
6. Anita, A., Mehta, R. and Mali, G. (2008). A review on anthelmintic plants. Natural Product Radiance, 7(5), 466-475.
7. Arenas, P. (1987). Medicine & magic among the Maka Indians of the Paraguayan Chaco. J. Ethnopharmacol., 21(3), 279-295.
8. Balfour, D.J.K. and Fagerstrom, K.O. (1996). Pharmacology of nicotine and its therapeutic use in smoking cessation and neurodegenerative disorders. Pharmacol. Ther., 72, 51-81.
9. Ban, N. and Cliffton, E.E. (1960). The effect of momentary Hyperlipemia on thrombolysis in-vivo. Thromb. Diath. Haemorrh., 4, 149.
10. Bapalal, G.V., and Adarsha, N. (2009). Chaukhambha Bharati Academy. 2, 146.
11. Barrett, B. (1994). Medicinal plants of Nicaragua'satlantic coast. Econ. Bot., 48(1), 8-20.
12. Barua, R.S. and Ambrose, J.A. (2013). Mechanisms of coronary thrombosis in cigarette smoke exposure. Arterioscler. Thromb. Vasc. Biol., 33, 1460-1467.
13. Bhat, R.B., Adeloye, A.A. and Etejere, E.O. (1985). Some medicinal plants of Nigeria. J. Economic and Taxonomic Botany, (6)1, 161-165.
14. Bhattarai, N.K. (1992). Medical ethnobotony in the Karnali zone, Nepal. Econ. Bot., 46(3), 257-261.
15. Binorkar, S.V. and Jani, D.K. (2012). Traditional medicinal usage of tobacco-A Review. Spatula, DD, 2(2), 127-134.
16. Borio, G. (2010). http://www.tobacco.org/resources/history/Tobacco_History.html
17. Brookes, J.E. (1937). Tobacco: it's history illustrated by the books, manuscripts and drawings and engravings in the lbrary of George Arents Jr. 1, 1507-1615.
18. Brookes, J.E. (1952). The mighty leaf: tobacco through the centuries. Boston: Little, Brown. 2-49.
19. Bussmann, R.W. and Sharon, W. (2006). Traditional medicinal plant use in Northern Peru: tracking two thousand years of healing culture. J. Ethnobiol. and Ethnomed., 2(47), 1-18.
20. Caceres, A.B., Giron L.M., Alvarado, S.R. and Torres, M.F. (1987a). Screening of antimicrobial activity of plants popularly used in Guatemala for the treatment of dermatomucosal diseases. J. Ethnopharmacol., 20(3), 223-237.
21. Caceres, A.B., Giron, L.M. and Martinez, A.M. (1987b). Diuretic activity of plants used for the treatment of urinary ailments in Guatemala. J. Ethnopharmacol., 19(3), 233-245.
22. Caceres, A.B., Lopez, B.R., Giron, M.A. and Logemann, H. (1991). Plants used in Gutemala for the treatment of dermatophytic infections. I. Screening for antomycotic activity of 44 plant extracts. J. Ethnopharmacol., 31(3), 263-276.
23. Charlton, A. (2004). Medicinal uses of tobacco in history. J.R. Soc. Med., 97, 292-296.
24. Charlton, A. and Moyer, C.A. (1991). Children and tobacco: the Wider View. Geneva: International Union against Cancer. 25-26.
25. Chase, M.W., Knapp, S., Cox, A.V., Clarkson, J.J., Butsko, Y., Joseph, J., Savolainen, V. and Paronny, A.S. (2003). Molecular systematics, GISH and the origin of hybrid taxa in *Nicotiana* (Solanaceae). Ann. Bot., 92(1), 107-127.
26. Cheeta, S., Kenny, P.J. and File S.E. (2000). Hippocampal and septal injections of nicotine and 8-OH-DPAT distinguish among different animal tests of anxiety. Prog. Neuropsychopharmacol. Biol. Psychiatry, 24, 1053-1067.
27. Clausen, R.E. (1928). Interspecific hybridization in Nicotiana. VII. The cytology of hybrids of the synthetic species, digluta, with its parents, glutinosa and tabacum. Univ. Cal. Pub. Botany, 11(10), 177-211.

28. Coee, F.G. (1996). Ethnobotony of Garifuna of eastern Nicargua. Econ Bot., 50(1), 71-107.
29. Comerford, S.C. (1996). Medicinal plants of two Mayan healers from SanAndres Peten Guatemala. Econ Bot., 50(3), 327-336.
30. Desmarchelier, C. (1996). Ritual & medicinal plants of the Eseejas of Amazonian rainforest. J. Ethnopharmacol., 52(1), 45-51.
31. Dickson, S.A. (1954). Panacea or precious bane. Tobacco in 16th century literature. New York: New York Public Library.
32. Eisen, M.E. (1958). Effect of vitamin-A, niacin and riboflavin on vascular lesions. A preliminary report. Am. J. Surge., 95, 438.
33. Feinhandler, S.J., Fleming, H.C. and Monahan, J.M. (1979). Pre-Columbian tobaccos in the Pacific. Econ. Bot., 33, 213-216.
34. Flores, J.S. (1996). The secretions and exudates of plants used in Mayan traditional medicines, J. Herbs Spices Medicinal Plants, 4(1), 53-59.
35. Fowles, J. (2003). Chemical composition of tobacco and cigarette smoke in two brands of New Zealand cigarettes. Final Report. New Zealand Ministry of Health. 3-4.
36. Francis, P., Palmer, A., Snape, M. and Wilcock, G. (1999). The cholinergic hypothesis of Alzheimer disease: a review of progress. J. Neurol. Neurosurg. Psychiatry, 66, 137-47.
37. Gambo, I.M., Galam, N.Z., Adamu, G., Ayaka, L.O., Habeeb, A.A., Bello, M.M., Bello, N., Rabiu, A.M. and Odeh, S.O. (2013). The effect of aqueous leave extract of *Nicotiana Tabacum* (tobacco) on some reproductive parameters and micro-anatomical architecture of the testis in male albino wistar rats. J. Natu. Sci. Res., 5(3), 137-143.
38. Giannopoulou, C., Kamma, J.J. and Mombelli, A. (2003). Effect of inflammation, smoking and stress on gingival crevicular fluid cytokine level. J. Clin. Periodontol., 30, 145-153.
39. Giron, L.M., Freire, V., Alonzo, A. and Caceres, A. (1991). Ethano botanical survey of the medicinal flora used by the Caribs of Gutemela. J. Ethnopharmacol., 34(2-3), 173-187.
40. Grassi, B. and Caltabiano, S. (1956). Effetto della Fatica, del Fumoe della Perfrigerazione su la Coagulatione del Sangue. Rass. Fisiopat. Clin. Therap., 28, 755.
41. Greer, J. and Poulson, T.C. (1983). Oral tissue alterations associated with the use of smokeless tobacco by teenagers. Oral. Surg. Oral. Med. Oral. Pathol., 56, 275-284.
42. Grieve, M. (1995). A modern herbal. Tobacco. Botanical.com.
43. Groark, K.P. (2010). The angel in the gourd: ritual, therapeutic, and protective uses of tobacco (Nicotiana tabacum) among the Tzeltal and Tzotzil Maya of Chiapas, Mexico. J. Ethnobiol., 30(1), 5-30.
44. Haber, J. (1994). Smoking is a major risk factor for periodontitis. Curr. Opin. Periodontol., 1, 12-18.
45. Harboume, J.B. (1991). Phytochemical methods, *A Guide to modern techniques of plant analysis 2nded, chapman and Hall, London.* 1-3, 84-86, 222-236.
46. Hedberg, I.O. (1983). Inventory of plants used in traditional medicine in Tanzania II, Plants of the Families Dilleniaceae-Opilliaceae. J. Ethanopharmacol., 9(1), 105-127.
47. Hirschmann, G.S., De-Arias, A.R. (1990). A survey of medicinal plants of minas gerais, Brazil. J. Ethnopharmacol., 29(2), 159-172.
48. Holdsworth, D. and Balun, L. (1992). Medicinal plants of the East & West Sepik Province, Papua new Guinea. Pharmaceutical Biol., 30(3), 218-222.
49. Holdsworth, D. and Sakulas, H. (1987). Medicinal plants of the Morobe province. Part II. The Aseki valley, Inter. J. Crude Drug Res., 25(4), 209-215.
50. Horwitz, o. and Waldorf, D.S. (1960). Effect of tobacco smoking on the clotting process in man as measured by Thromboelastography. Circulation, 22, 765.
51. Hussey, J.S. (1974). Some useful plants of early New England. Econ Bot., 28(3), 311-337.
52. Ilham, M. (1995). Tumor promoting activity of plants used in Malaysian traditional medicine. Nat. Prod. Sci., 1(1), 31-32.
53. Jahn, R. (1954). Tobacco Dictionary; J. C. Robert, *The Story of Tobacco in America* (1967); E. R. Billings, *Tobacco* (1875, repr. 1973); I. Gately, *Tobacco: The Story of How Tobacco Seduced the World* (2002).
54. Johannes, J., Jawes, J.J., Uma, S., Hayan, D., Luis, F.F. and John, P.L. (2002). Nicotine accelerates angiogenesis and wound healing in genetically diabetic mice. Am. J. Pathol., 161, 97-104.
55. Karvonen, M., Orma, E., Keya, A., Fidanza, F. and Brozek, J. (1959). Cigarette smoking: Serum cholesterol, blood pressure and body fatne. observations in Finland. Lancet, 1, 492.

56. Kershbaum, A., Khorsandian, R., Caplan, R.F., Bellet, and Feinberg, L.J. (1963). The role of catecholamines in the free fatty acid response to cigarette smoking. Circulation, 28, 52.
57. Khalifa, A.E. (2001). *Hypericum perforatum* as a nootropic drug, enhancement of retrieval memory of a passive avoidance conditioning paradigm in mice. J. Ethnopharmacol., 76(1), 49-57.
58. Knapp, S., Chase, M.W. and Clarkson, J.J. (2004). Nomenclatural changes and a new sectional classification in Nicotiana (Solanaceae). Taxon., 53(1), 73-82.
59. Landoni, J.H.D. (1990). Nicotiana tabacum linne. http://www.inchem.org/documents/pims/plant/nicotab.
60. Leete, E. (1983). Biosynthesis and metabolism of tobacco alkaloids. Alkaloids: chemical & biological perspectives–John Wiley & Sons, NY; 85-152.
61. Lip, G.Y., Kamath, S. and Hart, R.G. (2002). ABC of antithrombotic therapy: Antithrombotic therapy for cerebrovascular disorders. BMJ, 325(7373), 1161-1163.
62. Loewenthal, R. and Peer, J. (1991). Traditional methods used in the treatment of ophthalmic diseases among the Turkana tribe in northwest Kenya. J. Ethnopharmacol., 33(3), 227-229.
63. Luna, L.E. (1984). The concept of plants as teachers among four mestizo shamans of iquitos, northwestern Peru; J. Ethnopharmacol., 11(2), 135-156.
64. Maheshwari, K.K. (2012). Drugs Pharmacology, Ist edition, Ganglionic stimulating agents. Vallabh Prakashan, New Dehli, Ist edition, 56-57.
65. Martinez, G.J. and Lujan, M.C. (2011). Medicinal plants used for traditional veterinary in the Sierras de Cordoba (Argentina): An ethnobotanical comparison with human medicinal uses. J. Ethnobiol. Ethnomed., 2011; 7(1):23.
66. Maxwell, I.E. and Omeh, S.Y. (2010). Anti-nociceptive activity of the methanolic leaf of *Nicotiana tabacum (LINN).* Wilolud J*.,* 3, 5-10.
67. Moller, M.S. (1961). Pregnancy & child bearing in Tanzania. J. Trop Pediatrics Afr. Child health, 7(3), 66-78.
68. Nagraju, N. and Rao, K.N. (1990). A survey of plant crude drugs of Rayalseema, Andhra Pradesh India. J. Ethnopharmacol., 29(2), 137-158.
69. Nan-Ren, and Michael, P.T. (2001). AFLP analysis of genetic polymorphism and evolutionary relationships among cultivated and wild Nicotiana species. Genome, 44(4), 559-571.
70. Noguchi, M., Sakum, H. and Tamaki, E. (1968). The isolation & identification of Nicotianine, a new amino acid from tobacco leaves. Phytochem., 7(10), 1861-1866.
71. Peto, R., Lopez, A.D., Boreham, J., Thun, M., Heath, C.J. and Doll, R. (1996). Mortality from smoking worldwide. Br. Med. Bull., 52(1), 12-21.
72. Ramirez, V.R. (1988). Vegetales empleadosen medicina tradicional norperuana. Banco Agrario del peru & NACL Univ Trujillo, Peru. 54.
73. Rawat, A. and Mali, R.R. (2013). Phytochemical properties and pharmacological activities of *Nicotiana Tabacum*: A Review. Indian J. Pharmaceut. Biol. Res., 1(1), 74-82.
74. Reddy, K.S. and Gupta, P.C. (2004). Report on tobacco control in India-executive summary supported by Ministry of Health & Family Welfare, Government of India. New Delhi. 1-5.
75. Roberts, D.L. and Rohde, W.A. (1972). Isolation and Identification of flavor components of burley tobacco. Tobacco Sci., 16, 107-112.
76. Rodu, B. and and Ou, B. (2004). The antioxidant properties of tobacco. Tobacco Sci., 44, 71-73.
77. Roig, Y. and Mesa, J.T. (1945). Plantas medicinales, aromatic as o Venenosas de cuba. Ministerio de Agricultura, republica de Cuba, Havana. 872.
78. Roud, B. and Ou, B. (2004). The Antioxidant Properties of Tobacco. Tobacco Science, 44, 71-73.
79. Rowsell, H.C., Hegardt, B., Downie, H.G., Mustard, J.F. and Murphy, E.A. (1966). Adrenaline and experimental Thrombosis. Brit. J. Haemet., 12, 1.
80. Sairam, K., Rao, C. and Goel, R. (2001). Effect of *Convolvulus pluricautis* Chois on gastric ulceration and secretion in rats. Indian J. Exp. Biol., 39, 350-354.
81. Scerri, C. (2005). Nicotine: Pharmacology and therapeutic implications in neurodegenerative and psychiatric disorders. Malta Med. J., 1(4), 17-21.
82. Schmeda-Hirschmann, G. and De-Arias, A.R. (1992). A screening method for natural products on triatomine drugs. Phytother Res., 6(2), 68-73.

83. Schultes, R.E. (1995). The healing forest: medicinal & toxic plants of the northwest Amazonia. Dioscorides Press, Portland. 432-436.
84. Shaligram, V.L. and Nighantubhushanam, S. (2004). Khemraj Krishnadas Prakashan Mumbai. 4th Edition, 908.
85. Singh, V.K. (1996). Ethnomedicines in the Bahraich district of Uttar Pradesh, India. Fitoterapia, 67(1), 67-76.
86. Singh, Y.N. (1986). Traditional medicine in Fiji: Some herbal folk cures by Fiji Indians. J. Ethnopharmacol., 15(1), 57-88.
87. Sivanandam. (2010).Social pathology in modern world. Problems of tobacco, smoking and chewing. http://sivanandamsw.blogspot.in.
88. Stedman, R.L. (1968). The chemical composition of tobacco and tobacco smoke. Chem. Rev., 68(2), 153-207.
89. Stewart, G.G. (1967). A history of the medicinal use of tobacco 1492–1860. Med. Hist., 11, 228–268.
90. Tabata, M. (1994). Traditional medicine in Turkey III. Folk Medicine in east Anatolia, Van and Biltis province. Int. J. Pharmacog., 32(1), 3-12.
91. The biggest plant dictionary. (2011). Nicotiana tabacum: Ethanomedicinal uses: http://thebiggestplantdictionary.blogspot.in/
92. The Columbia Electronic Encyclopedia, 6th ed. (2012). Columbia University Press.
93. The Columbia Encyclopedia (2008). The Columbia Encyclopedia, 6th (Ed.), Columbia University Press.
94. Thoma, C.B. (1960). Characteristics of smokers compared with nonsmokers in a population of healthy adults, including observations on family history, blood pressure heart rate, body weight, cholesterol and certain psychological trait. Ann. Int. Med., 53, 697.
95. Trease, W. and Evans, C. (1996). Pharmacology, Bailliere tindall, London. 113th; 89-122, 313-544.
96. Vanio, H. (1986). Tobacco and cancer. Cancer Res., 46(1), 444-447.
97. Viesca-Trevino C. Estudios sobre ethenobotanica anthropologia medica. Inst Mexicano para est pl Medic, Mexico. 1976.p.104
98. Weniger, B.M. (1986). Popular medicine of the central plateau of Haiti, Ethanopharmacological inventory. J. Ethnopharmacol., 17(1), 13-30.
99. Wennig, R. (2009). Back to the roots of modern analytical toxicology: Jean Servais Stas and the Bocarme murder case. Drug Test Anal., 1(4), 153-155.
100. Wenzel, D.G. and Singh, T. (1962). Effect of nicotine and epinephrine on in-vivo coagulation time in rabbits. J. Pharm. Sci., 51, 875.
101. Wenzel, D.G., Kamal, J.S. and Turner, J.A. (1960). The chronic effects of orally administered nicotine in cholesterol-Fed rabbits. Ann. New York Acad. Se., 90, 302.
102. Wenzel, D.G., Turner, J.A., Jordan, S.W. and Singh, J. (1961). Cardiovascular interaction of nicotine, ergonomine and hypercholesterolemia in the rabbit. Circulation Res., 9, 694.
103. West, R.J. and Russell, M.A. (1985). H. Nicotine pharmacology and smoking dependence; Oxford University Press, Oxford. 303-314.
104. Xie, W., Zhang, X., Wang, T. and Hu, J. (2012). Botany, traditional uses, phytochemistry and pharmacology of Apocynum *venetum L*. (Luobuma): A review. J. Ethnopharmacol., 141(1), 1-8.
105. Zaidi, M.I., Wattoo, F.H., Wattoo, M.H.S. and Tirmizi, S.A. (2012). Antibacterial activities of nicotine and its Zinc complex. African J. Microbiol. Res., 6(24), 5134-5137.
106. Zargari, A. (1992). Medicinal plants, Tehran University Publications. 5, 3, 889.

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