

## Effective Replacement Therapy by Aid of Nicotine

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**ABSTRACT:** Cigarette smoking affects each part of organs of Human beings and it causes diseases and affects their health. Quitting smoking will help to lower the risk associated by smoking related health issues. This can be achieved by nicotine replacement therapy by the aid of nicotine products. Nicotine is a stimulant and potent para sympathomimetic alkaloid that is naturally produced in the nightshade family of plants. It is used for the treatment of tobacco use disorders as a smoking cessation and nicotine dependence for the relief of withdrawal symptoms. Nicotine is considered to be a safer alternative of tobacco. It will help to stop smoking by supply of low dose of nicotine. Types of Nicotine Replacement Therapy include the adhesive patch, chewing gum, lozenges, nose spray, and inhaler. The various herbal formulation and Homeopathic products helps in the withdrawal of nicotine. The present study to review pharmacological activities of *Nicotiana tabacum* and various products available in market for nicotine withdrawal therapy .

**KEY WORDS:** Tobacco, Nicotine, Replacement therapy

### I. INTRODUCTION:

Tobacco plant is a perennial, erect glandular-pubescent herb. *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 semi-amplexicaul and decurrent and long trumpet shaped white-pinkish, rosy or reddish flowers, pedicelled, 4-5 cm long, in many flowered, usually paniced 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. *Nicotiana tabacum* have analgesic activity, anesthetic activity, angiogenesis inhibition, antibacterial activity, anti convulsant activities, anti estrogenic effect, antifungal activity, antiglaucomic activity, antioxidant activity, antistress effect antiviral activity, aromatase inhibition, arrhythmogenic effect, carcinogenic activity[1] Nicotine is used for treatment of Alzheimer disease, Parkinson disease, depression and anxiety, schizophrenia, attention deficit hyperactivity disorder (ADHD), pain, and obesity.[2]



Fig:1 Tobacco leaf

Table1:TAXONOMIC CLASSIFICATION:[3]

Scientific name:	Nicotiana Tabacum Linn
Kingdom:	Plantae, Eudicots, Asterids
Order:	Solanales
Genus:	Nicotiana
Species:	Nicotianatabacum
Division:	Magnoliophyta
Family:	Solanaceae

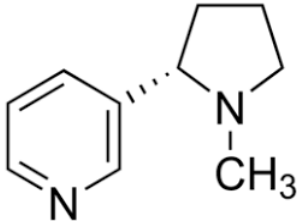
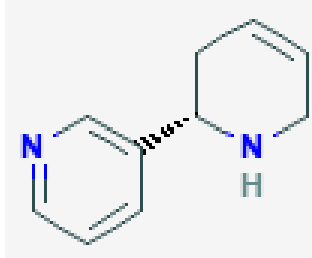
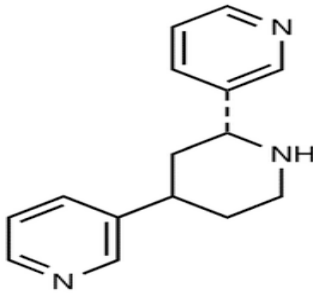
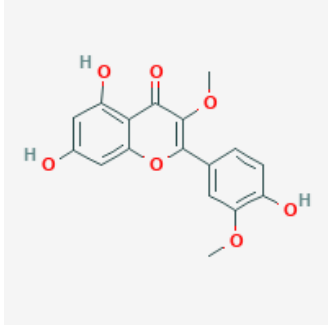
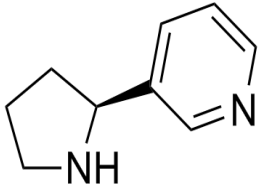
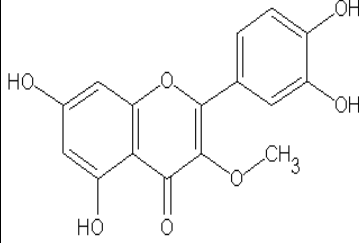
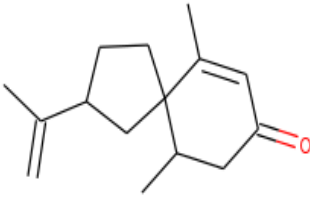
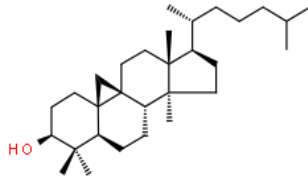
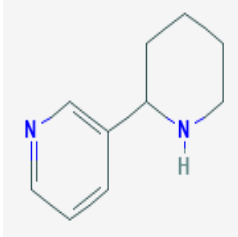
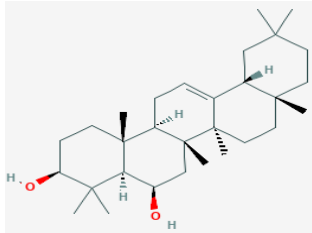


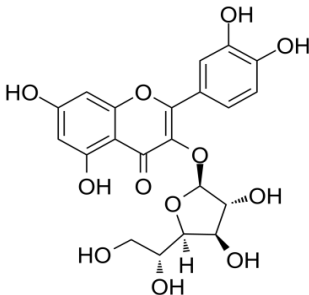
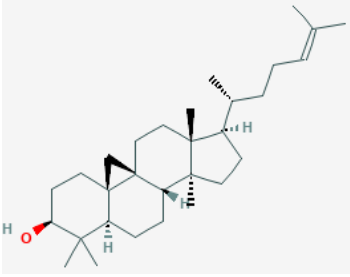
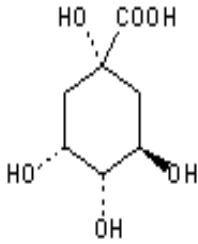
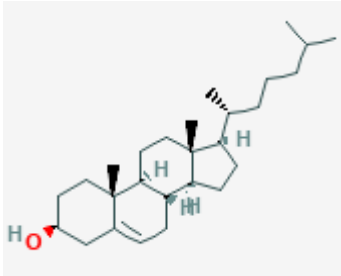
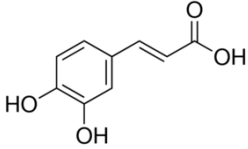
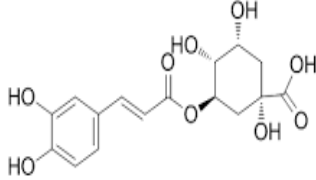
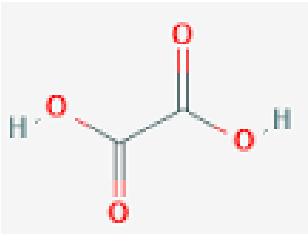
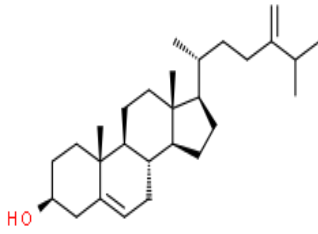
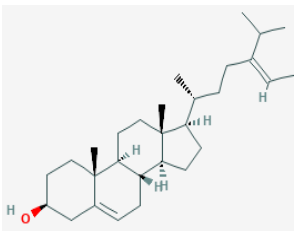
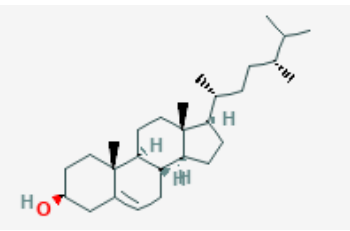
**Fig: 2: Picture Dipping Different parts of *Nicotiana tabacum***

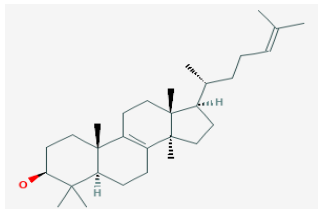
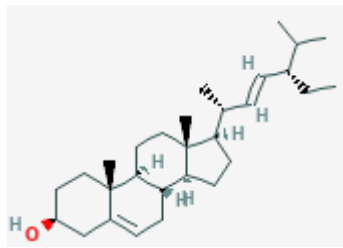
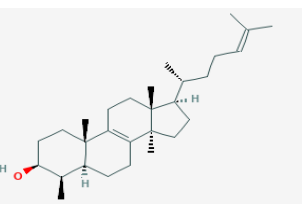
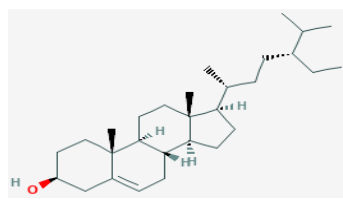
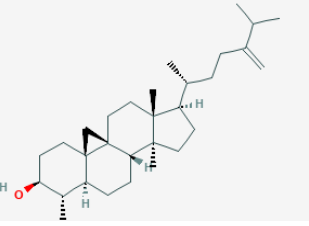
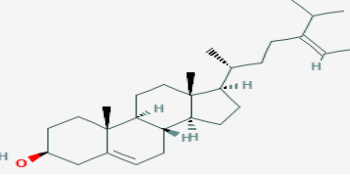
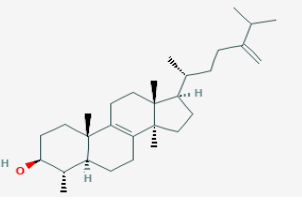
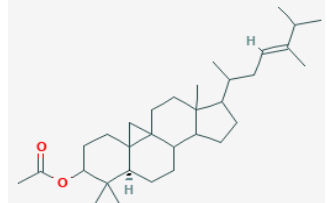
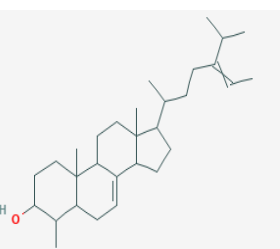
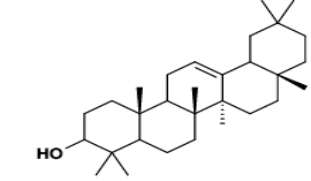
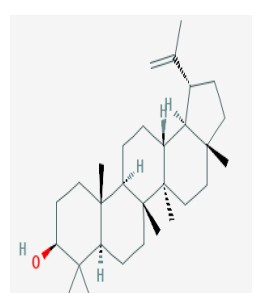
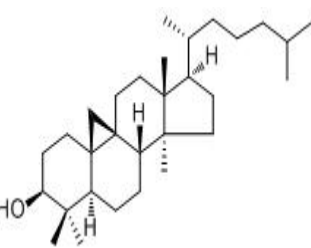
**Table 2: Common & Vernacular names:[4]**

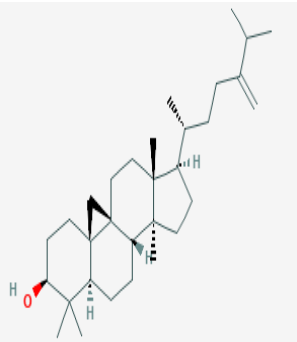
<b>Latin names</b>	Nicotiana tabacum
<b>Common names</b>	Fumo, Petume, Petina, Pitura, Etum, Tabaco, Tobacco, Tabaci Folia
<b>Synonyms</b>	Tabacca, Tabaci Folia, Tobacco, Tamak, Siah (Marma).
<b>Arabic</b>	Tanbak
<b>English</b>	Tobacco
<b>Hindi</b>	Bhambakhu, bujjerbhang, hoge-soppu, tamakhu, tamaku, tamarkut, tambaka, tambakhu, tambaku, tampaku, tanbaku, tumak
<b>Kannada</b>	Beedihooranayele, cigaretuyelegida, hogesoppu, hogesappu, hogesoppu, tambaku, thambaaku
<b>Malayalam</b>	pokala, puka-yila, pukayil, pukayila
<b>Marathi</b>	pan, tamaku, tambaku, thamaaku, thambaaku
<b>Persian</b>	Tanbaku
<b>Sanskrit</b>	Dhumapatram , dhumrapatra, dhumrapatrika, gucchaphala, kalanja, krimighni, ksarapatra, ksharapatra, tamakhu, tamakhuh, tamala, tamrakuta, tamrakuttika, tamraparna, vajrabhringi, vajrabhrngi
<b>Tamil</b>	Auritayavilai, avipattiram, avippattiram, biramam, birammappattiram, inkariyam, irutticinkam, kanananti, kanananti, kariyakoracceti, kariyakoram, karuncurai, kentuvallikacceti, kentuvallikam, koram, kotikkaraiccerivu, maccankolli, maccankollicceti, nattuppukaiyilai, paccaipukaiyilai, paityankari, piramam, piramapattiram, piramapattiri, pirammappattiram, pittakori, pogheielley, pugaielai, pugai-ilai, pugaielai,
<b>Telugu</b>	Dhoomrapathramu, dhumra-patramu ,dhumrapatramu, pogaaku, pogaaku, pogaku
<b>Urdu</b>	tambaku, tambakusurti

Table 3: PHYTOCHEMICAL CONSTITUENTS:[5]

Constituents	Structure	Constituents	Structure
Nicotine		Anatabine	
Anatalline		Quercetin-3,3'-dimethyl ether	
Nornicotine		quercetin-3-Me ether	
solavetivone.		cycloartanol,	
Anabasine		24-daturadiol	

<p>Isoquercitrin</p>		<p>Cycloartenol</p>	
<p>Quinic acid</p>		<p>Cholesterol</p>	
<p>1-, caffeic acid</p>		<p>chlorogenic</p>	
<p>oxalic acid</p>		<p>24-methylenecholesterol</p>	
<p>28- isofucosterol</p>		<p>campesterol</p>	

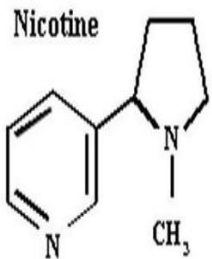
Lanosterol		Stigmasterol	
31- norlanosterol		Sitosterol	
Cycloeucalenol		28- isofucosterol	
Obtusifoliol		31-norcycloartenol	
Citrostadienol		$\beta$ -amyrin	
Lupeol		cycloartanol	

24-methylenecycloartanol			
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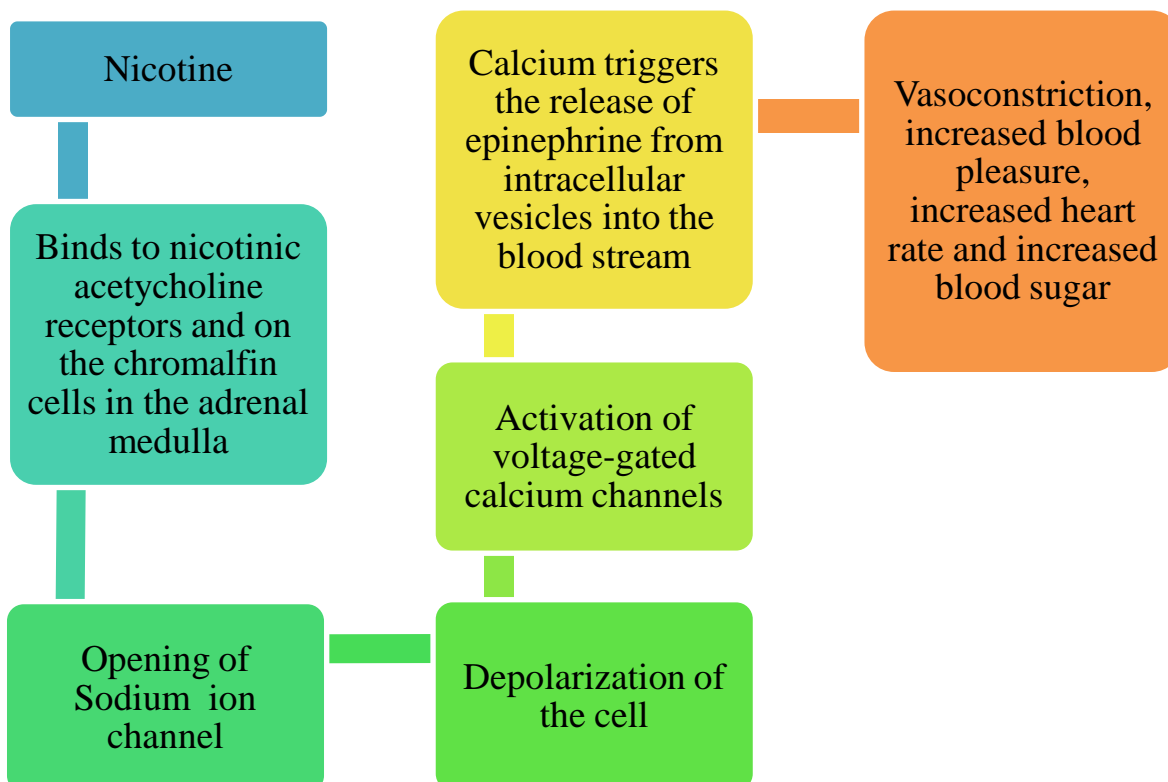
**Table 4: Reported Pharmacological Activities of *Nicotiana tabacum*:**

Topic	Proven activity	Parts used	report	Reference
Antibacterial activities of nicotine and its zinc complex	Antibacterial activities	Leaves	zinc (II) complex of nicotine is more active against different types of bacterial strains as compared to zinc metal salt and nicotine alone	[6]
Anti –Nociceptive Activity of The Methanolic leaf of <i>Nicotiana tabacum</i> (LINN)	Anti-nociceptive activity	Leaves	Methanolic leaf extract of <i>Nicotiana tabacum</i> showed significant antinociceptive activity	[7]
Screening of crude extracts of twelve medicinal plants and “wondercure” concoction used in Nigeria unorthodox medicine for activity against <i>mycobacterium tuberculosis</i> from tuberculosis patients sputum.	Antimicrobial activity	Whole Plant	Aqueous and ethanolic extract of <i>nicotiana tabacum</i> used as medicinal plant extract in treatment of tuberculosis.	[8]
In vitro and In vivo anthelmintic activity of <i>Nicotiana tabacum</i> L. leaves against gastrointestinal nematodes of sheep.	Anthelmintic activity	Leaves	Methanolic extract shows greater anthelmintic activity than aqueous extract	[9]
A Novel Pathogen- and Wound-Inducible Tobacco ( <i>Nicotiana tabacum</i> ) Protein with Antifungal Activity	Anti fungal activity	Leaves	Protein purified from <i>Nicotiana tabacum</i> shows synergetic action with both a tobacco class I chitinase and a class I 8-1,3-glucanase.	[10]

II) TABLE: 5: PHYSIOCO-CHEMICAL CHARACTERISTICS OF NICOTINE:[11]

STRUCTURE	CHEMICAL NATURE	PHYSICAL NATURE	PHARMACOKINETIC PARAMETERS:
 <p>Nicotine</p>	<b>Its formula</b> : C <sub>10</sub> H <sub>14</sub> N <sub>2</sub>	<b>Nature</b> hygroscopic	<b>Absorption:</b> Absorption of nicotine through the buccal mucosa is relatively slow
	<b>Molar mass</b> :162.23grams/Mol	<b>Colour:</b> colourless to yellow-brown.	<b>Volume of distribution:</b> 2 to 3 L/kg
	<b>Melting point</b> :79 degree C{-110 degree F}	<b>Odour:</b> Strong of tobacco	<b>Protein binding:</b> Less than 5%
	<b>Addiction liability:</b> High	<b>Solubility:</b> alcohol, ether, light petroleum	<b>Metabolism:</b> Primarily hepatic, cotinine is the primary metabolite. primarily hepatic CYP2A6, CYP2B6, FM03
	<b>Flash point:</b> 95 <sup>0</sup> C		<b>Route of elimination:</b> About 10% of the nicotine absorbed is excreted unchanged in the urine. urine {10-20% {gum}}, PH dependent, 30% {inhaled} 10-30%
	<b>Auto-ignition temperature:</b> 244 <sup>0</sup> C		<b>Half life:</b> Cotinine has a half life of 15-20 hours, while nicotine has a half life of 1-3 hours
			<b>Clearance:</b> 1.2 L/min

Flow chart 1: MECHANISM OF ACTION:[12]



**Table 6: Negative Health Effects Of Nicotine:[13]**

Disease	Complication
Lung cancer & Other lung cancer	<ul style="list-style-type: none"> <li>• 9 out of 10 lung cancer cases.</li> <li>• Emphysema and chronic bronchitis esophagus, larynx, throat (pharynx) and mouth and is related to cancers of the bladder, pancreas, kidney and cervix, and some leukemias.</li> <li>• Overall, smoking causes 30 percent of all cancer deaths</li> </ul>
Heart& circulatory system problems	<ul style="list-style-type: none"> <li>• Increases your risk of dying of heart and blood vessel (cardiovascular) disease, including heart attack and stroke.</li> <li>• smoking just one to four cigarettes daily increases your risk of heart disease</li> <li>• Stopping smoking reduces your risk of having a heart attack by 50 percent in the first year.</li> </ul>
Diabetes	<ul style="list-style-type: none"> <li>• Increases insulin resistance, which can set the stage for the development of type 2 diabetes</li> <li>• kidney disease and eye problems.</li> </ul>
Eye problems	<ul style="list-style-type: none"> <li>• cataracts and loss of eyesight from macular degeneration.</li> </ul>
Infertility and impotence	<ul style="list-style-type: none"> <li>• risk of reduced fertility in women and the risk of impotence in men.</li> </ul>
Pregnancy and newborn complications	<ul style="list-style-type: none"> <li>• higher risk of miscarriage, preterm delivery, lower birth weight and sudden infant death syndrome (SIDS) in their newborns.</li> </ul>
Cold, flu and other illnesses	<ul style="list-style-type: none"> <li>• respiratory infections, such as colds, flu and bronchitis.</li> </ul>
Physical appearance	<ul style="list-style-type: none"> <li>• change the structure of skin, premature aging and wrinkles. yellows stain in teeth, fingers and fingernails.</li> </ul>
Teeth and gum disease	Increased risk of developing inflammation of the gum (gingivitis) ,periodontitis).

**Flow chart:2: TYPES OF NICOTINE PRODUCTS[14]**





TABLE 7 : METHODS USED TO QUIT FROM NICOTINE ADDICTION[15]

A. Nicotine replacement therapy	B. Non-nicotine therapies (medications)	C. Novel therapies	D. Behavioural treatments
Nicotine transdermal patch systems	Bupropion (Zyban), GlaxoSmithKline	Anti smoking vaccine (Nic Vax)	Lobelia
Nicotine nasal spray	Varenicline, Pfizer	Green smoke electronic cigarette	Vitamin B and C
Nicotine delivery through the oral mucosa	Nortriptyline		Make a list
	Clonidine		Use as app to track habits
	Vaccines		



**A. Nicotine replacement therapy (NRT):**

Nicotine in cigarettes is addictive, which is why people experience unpleasant withdrawal symptoms when they try to quit. Nicotine replacement therapy (NRT) provides a low level of nicotine without the other poisonous chemicals in tobacco smoke.



Flow chart: 3: Nicotine replacement therapy formulations:



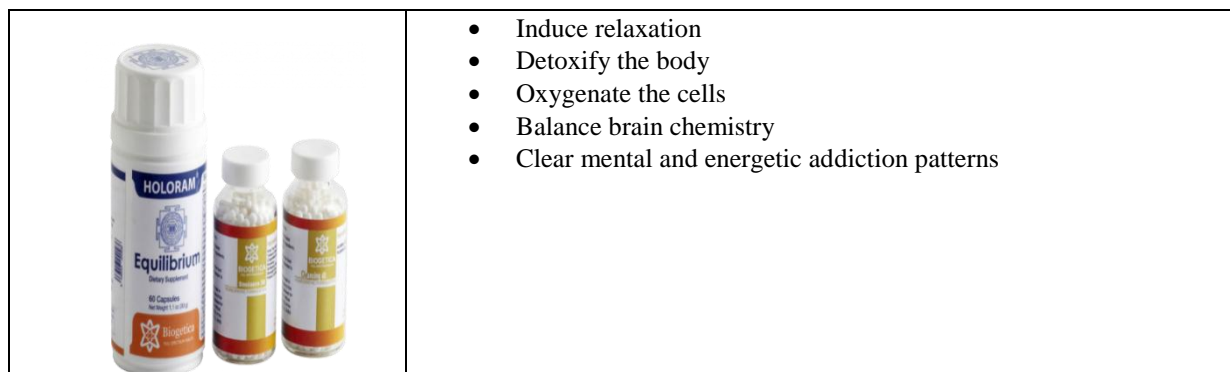
**TABLE 8: HERBAL FORMULATION: [16]**

HERBAL FORMULATION	DOSE	USE	Image
QUIT TEA	3 to 5 minutes in boiling water	<ul style="list-style-type: none"> <li>• Increase Energy &amp; Reduce Hunger.</li> <li>• help to cleanse lungs naturally and detoxify themselves</li> </ul>	
QUIT WTR	4 TO 8 SHOTS	<ul style="list-style-type: none"> <li>• Easy to use, works fast, takes away the urge to smoke, can help reduce stress or anxiety.</li> <li>• Help you curb cravings and stop smoking</li> </ul>	

**TABLE 9: Homeopathic Product: [17]**

Products	Uses
	<ul style="list-style-type: none"> <li>• Contains Natrium Chloatum, Robinia &amp; Tabacum to address other withdrawal symptoms like headache, paleness, perspiration, cold limbs etc</li> <li>• Dosage: 15-20 drops in some water 3 times daily. Safe, free of any side effects.</li> </ul>
	<ul style="list-style-type: none"> <li>• SBL Daphne Indica 1X Tablets is Indicated for Tobacco addiction and associated complaints like decreased appetite, raised blood pressure, sweating, nausea and diarrhoea</li> <li>• Composition: Each tablet contains 250 mg of <i>Daphne indica</i></li> <li>• Dosage: Adults: 2 tablets three times daily or as prescribed by the physician.</li> </ul>

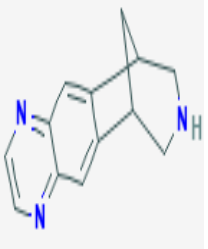
 <p>Aniel Homeopathic Medicine DCA's Formula for Smoking De-Addiction 3 X 1 month medicine (approx.)</p>	<ul style="list-style-type: none"> <li>• Dose: Take 4 globules each, before breakfast and dinner.</li> <li>• This homeopathic formula eliminate tobacco from patient's body, helps in reducing it's craving and creates a distaste for tobacco in the body.</li> </ul>
 <p>ALCOBAN DROP</p>	<ul style="list-style-type: none"> <li>• The substances used in Alcoban detoxify the body for toxic materials deposited in the system from prolonged use of any such substance.</li> </ul>
 <p>Daphne indica 1x Schwabe HOMOEOPATHIC MEDICINE</p>	<ul style="list-style-type: none"> <li>• It works at the safest and deepest level to help you in smoking cessation.</li> <li>• Composition: Each tablet contains 250 gm of Daphne Indica 1X</li> </ul>
 <p>Smoking Withdrawal Non-Habit Forming May help temporarily with* Tobacco &amp; Cigarette Cravings Nervous Tension Irritability Detoxification NatraBio 60 Tablets Natural Homeopathic Medicine</p>	<ul style="list-style-type: none"> <li>• Temporarily help you fight cigarette and tobacco cravings and manage unpleasant Our small, mild-tasting tablets dissolve quickly in the mouth for faster absorption and utilization.</li> </ul>
 <p>Stop-it Smoking NICOTINE FREE 2-Part Quit Smoking Kit Anti-Craving Lozenges Reduces Tobacco Cravings Calmes Nervous Tension Detoxifying Tablets Reduces Irritability Helps Detoxify NatraBio 48 Lozenges / 60 Tablets Natural Homeopathic Medicine</p>	<ul style="list-style-type: none"> <li>• Dissolve one lozenge in the mouth every 1-2 hours, or as needed whenever the desire for cigarettes or tobacco occurs.</li> <li>• Use: Reduces the craving for cigarettes and tobacco. Helps to temporarily relieve the nervous tension and irritability due to cessation of tobacco use.</li> </ul>

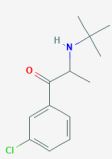
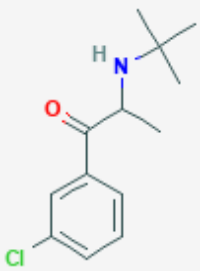
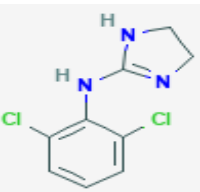


- Induce relaxation
- Detoxify the body
- Oxygenate the cells
- Balance brain chemistry
- Clear mental and energetic addiction patterns

**B) Drugs used in nicotine replacement therapy:[18]**

**TABLE 10:**

Drug/Structu	Trade name	Dose	Uses	Side effect
<p>Varenicline</p> 	Chantix Champix	<p>Days 1 to 3: 0.5 mg orally once a day</p> <p>Days 4 to 7: 0.5 mg orally 2 times a day</p> <p>Days 8 to end of treatment: 1 mg orally 2 times a day</p> <p>Duration of therapy: 12 weeks</p>	<p>Varenicline is a smoking cessation medicine. It is used together with behavior modification and counseling support to help you stop smoking.</p>	<p>a seizure (convulsions), strange dreams, sleepwalking, trouble sleeping;</p> <p>new or worsening mental health problems--mood or behavior changes, depression, agitation, hostility, aggression;</p> <p>heart attack symptoms--chest pain or pressure, pain spreading to your jaw or shoulder, nausea, sweating;</p> <p>stroke symptoms--sudden numbness or weakness (especially on one side of the body), slurred speech, problems with vision or balance.</p>

<p>Bupropion</p>  <p>Amfebutamone</p> 	<p>Wellbutrin &amp; Zyban</p>	<p>The initial dose of sustained-release tablets is 150 mg daily; target dose is 150 mg twice daily; maximum dose is 200 mg twice daily.</p> <p>The initial dose of extended-release tablets is 150 mg daily; target dose is 300 mg daily; maximum dose is 450 mg daily.</p>	<p>Bupropion is used for the management of major depression (major depressive disorder) and seasonal affective disorder (depression that occurs primarily during the fall and winter). It is also prescribed for smoking cessation.</p> <p>Off-label uses (non-FDA approved) for bupropion include posttraumatic stress disorder (PTSD), anxiety, attention deficit hyperactivity disorder (ADHD), social phobia, and nerve pain (neuropathic pain).</p>	<p>Weight loss, Skin rash, Sweating  Ringing in the ears (tinnitus), Shakiness, Stomach pain, Dizziness, Muscle pain, Fast heartbeat, Sore throat  Frequent urination, Agitation, Dry mouth, Insomnia, Headache, Nausea, Constipation, Tremor  In some people, the agitation or insomnia is most marked shortly after starting therapy.</p>
<p>Clonidine</p> 	<p>Catapres</p>	<p><i>injectable solution</i></p> <ul style="list-style-type: none"> <li>• 100mcg/mL</li> <li>• 500mcg/mL</li> </ul> <p><i>patch, extended-release</i></p> <ul style="list-style-type: none"> <li>• 0.1mg/day</li> <li>• 0.2mg/day</li> <li>• 0.3mg/day</li> </ul> <p><i>tablet, immediate-release</i></p> <ul style="list-style-type: none"> <li>• 0.1mg</li> <li>• 0.2mg</li> <li>• 0.3mg</li> </ul> <p><i>tablet, extended-release</i></p> <ul style="list-style-type: none"> <li>• 0.1mg</li> </ul>	<p>Clonidine extended-release tablets are used to treat symptoms of attention deficit hyperactivity disorder (ADHD). They can be used by people aged 6–18 years.</p>	<p>drowsiness, Dry mouth and dry eyes, dizziness, tiredness stomach upset or pain sedation, constipation, headache, upper respiratory tract infection, feeling irritable, trouble sleeping nightmare`s  Serious side effects increased then decreased blood pressure, slower or faster heart rate, uneven heart rate dizziness when you stand passing out, slowed breathing or trouble breathing, chest pain hallucinating.</p>

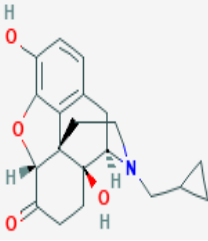
<p>Naltrexone Morphinan-6-one, 17-(cyclopropylmethyl)-4,5-epoxy-3,14-dihydroxy</p> 	<p>ReVia and Vivitrol</p>	<p>Tablet</p> <ul style="list-style-type: none"> <li>• 50mg microspheres for IM injection</li> <li>• 380mg</li> </ul>	<p>Naltrexone is used as part of a treatment program for drug or alcohol dependence.</p> <p>Naltrexone is used to prevent relapse in people who became dependent on opioid medicine and then stopped using it. Naltrexone can help keep you from feeling a "need" to use the opioid.</p> <p>Naltrexone is also used to treat alcoholism by reducing your urge to drink alcohol.</p>	<p>severe nausea, vomiting, or diarrhea; mood changes, confusion, hallucinations (seeing or hearing things); depression, thoughts about suicide or hurting yourself; or liver problems--nausea, upper stomach pain, itching, tired feeling, loss of appetite, dark urine, clay-colored stools, jaundice (yellowing of the skin or eyes). Common side effects may include: nausea, vomiting, stomach pain; headache, dizziness, drowsiness; feeling anxious or nervous; sleep problems (insomnia); or muscle or joint aches.</p>
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TABLE 11: VACCINES AVAILABLE:[19]

VACCINE NAME	Manufacturer	Completed phases	On going phases
NicVAX	GlaxoSmithKline/Nabi Biopharmaceuticals	Phase I & II	-
TA-NIC	Celtic pharmaceuticals	Phase II	Phase II
NIC002	CytosBiiotechnology/Novartis	Phase I & II	-
Niccine	Independent pharmaceutica	Phase I	Phase II (no data)
SEL-068	Selecta BiosciencesInc.		Phase I (no data)

**C.Novel therapies:**

**E-cigarettes :** An e-cigarette is an electronic device that allows for the inhalation of nicotine in a vapour without the other harmful by products of tobacco, such as tar and carbon monoxide.The e-cigarette may be less hazardous than tobacco for existing smokers, but it appears to bring dangers of its own.E-cigarettes claim to bypass many of the health risks of tobacco smoking, and to offer a more healthful alternative to cigarettes and



other conventional forms of nicotine intake.

**D.Behavioural treatments [16,20]**

**I) Lobelia :** Lobeline, the active ingredient in the lobelia plant, is thought to work by binding to the same receptor sites in the brain as nicotine, causing a release of dopamine, therefore helping with the mood swings and cravings that occur when stopping smoking.

**II) Vitamins B and C:**

The B vitamins are known as the "anti-stress" vitamins and they can help to balance mood.

Vitamin C is a powerful antioxidant that may help to protect the lungs from the oxidative stress caused by cigarette smoke.

**III) Use an app to track habits**

Quit smoking app on a tablet computer. Certain apps can help to track and cut down on smoking cigarettes.

These apps can help track smoking consumption and nicotine-craving cues; this information can then be used to plan when and where to reinforce a new healthy habit in place of the old unhealthy one.

• **AVAILABLE APP:**

**The Quitter's Circle**

•Is a quit smoking app, developed as a joint effort between the American Lung Association and Pfizer. The app provides daily tips to help ease your transition to nonsmoking. It also has tracking features, the ability to set goals, and allows you to build a “quit team” of friends and family who support your efforts.

**SmokefreeTXT**

•Another mobile app for helping smokers kick the habit comes from Smokefree. gov. Sign up on SmokefreeTXT to receive tips, advice, and encouragement via text message whenever you need it.

**Table 12: FORMULATION AND OTHER STUDIES BY NICOTINE:**

Proved effect	Formulation	Evaluation parameters	Reported Biological activity	Reference
Development and in-vitro evaluation of nicotine hard candy lozenges for smoking cessation	Nicotine hard candy lozenges	<ol style="list-style-type: none"> <li>1. Weight variation test</li> <li>2. Lozenge hardness</li> <li>3. Lozenge thickness</li> <li>4. Friability</li> <li>5. In vitro drug release studies</li> </ol>	Nicotine hard candy lozenges 2mg and 4mg with HPC 4% (NC11, NC25) were optimized. The optimized formulations showed 100% release within 30minutes	[21]
Effects of Nicotine-Free E-Cigarettes on Urges to Smoke and Cigarette Withdrawal Symptoms: A Randomised Cross-Over Study	Nicotine-free electronic cigarettes (EC)	Cross over study	EC reduced urge-to-smoke to a greater extent than SB . but this effect diminished by the evening.	[22]
A novel model mouth system for evaluation of In Vitro release of nicotine from moist snuf	Moist snuf	novel model mouth system	A novel model mouth system has been developed to evaluate release behaviour of tobacco constituents in pouch moist snuff.	[23]
The acute effects of daily nicotine intake on heart rate – A toxicokinetic and toxicodynamic modelling study	-	<ol style="list-style-type: none"> <li>1. toxico kinetic and toxicodynamic (PBTK/TD) modelling</li> </ol>	A joint PBTK–TD model for the Caucasian population, calibrated and validated by scenarios: cigarette smoking, oral and dermal absorption and their effects on acute increase in heart rate at rest and during exercise.	[24]

## II. CONCLUSION :

Nicotine is injurious to health and produce serious effects in human being . most popular way of consuming nicotine is by smoking cigarettes. There are more than 5,000 chemical components found in cigarette smoke and hundreds of them are harmful to human health, according to the Centers for Disease Control and Prevention. But alkaloid nicotine and its medicinal values are quite interesting and it has potential biological activities. Nicotine replacement therapy has key role to save human from tobacco products and its addicts. This paper will provide information to future scientist to design new formulations by using nicotine with less side effects.

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