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# TREATMENT OF TOBACCO DEPENDENCE IN SCIENTIFIC MANNER

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## ABSTRACT

In this current review, an endeavour has been made to explain the treatment of major health hazard i.e. Tobacco Dependence, the worldwide annual death number due to Tobacco Dependence is more than five million and some countries which shows Largest Tobacco Production (Annually). All the information has been gathered about the Tobacco (nicotine). An isolation method using fungal Pectinase to release Mesophillic cells and its further process is also highlighted. Nicotine is powerful drug that produce addiction. Tobacco Dependence is very dangerous to human health but still people are depending on it. It is the main cause of many Diseases like Mouth Cancer, Lungs Cancer, Cardiac diseases. Since it is considered to be a major health Hazard in the world and thus it is the second largest reason to 'death' in worldwide but it can be treated with FDA approved medication, Counseling and behavioral change programs with scientific manner.

**Keywords: Tobacco Dependence, Nicotine patches, Chemical Constituents, Treatment, Isolation, Cessation, Cigarette, Smoking**

## INTRODUCTION

Everybody knows that smoking is bad for the health. But do they really understand just how dangerous smoking is? Tobacco contains nicotine. It is a highly addictive drug that makes it difficult to smokers to kick the habit. Tobacco products also contain many poisonous and Harmful substances that cause disease and premature death. Tobacco use remains the leading preventable cause of disease, disability and mortality in the world, where it causes an estimated 480,000 deaths annually and accounts for approximately 90% of deaths from lungs cancer, 60% from pulmonary disease and 30% from Heart diseases. Worldwide, Tobacco use causes more than 5 million deaths per year. If the pattern of smoking all over the globe doesn't change, more than 8 million people a year will die from diseases related to tobacco use by 2030 **[1]**.

In India - One Million deaths occur annually, which is approximately 1/6$^{th}$ of the World's Tobacco related death (2019) – Notably, this figure is expected to go up to 1.5 million annually by 2020.

Current users of tobacco products are classified into four groups:-

- Exclusive combustible tobacco smokers excluding bidi's (39%); the majority were exclusive cigarette smokers (38%).
- Exclusive bidi smokers (7%)
- Exclusive smokeless tobacco users (30%); these users mainly consumed gutka (22%) and loose-leaf chewing tobacco (8%)
- Dual/poly products users (22%) product use include cigarettes (17%), bidis (14%), and gutka (11%)

31% of exclusive bidi smokers claimed they started smoking before the legal smoking age of 18 years.

19% of current cigarette smokers are moderately or highly dependent on nicotine (2019) **[1]**

**Global Tobacco Utilization**

19.2% of men, 2.0% of women and 10.7% (99.5 million) of all adults currently smoke tobacco.

29.6% of men, 12.8% of women and 21.4% (199.4 million) of all adults currently use smokeless tobacco.

42.4% of men, 14.2% of women and 28.6% (266.8 million) of all currently use tobacco (smoked /smokeless tobacco) **[2, 3]**.

**Secondhand Smoke**

38.7% of adults were exposed to second hand smoke at home.

30.2% of adults who works indoors are exposed to second-hand smoke at their workplace.

7.4% of adults were exposed to second hand smoke at restaurants **[2, 3]**.

**Knowledge Attitude and Perceptions**

92.4% of adults believed that smoking causes serious illness and 95.6% of adults believed that use of smokeless tobacco causes serious illness **[3]**.

**Top 10 Largest Tobacco Producing Countries (2019) in the World**

Top 10 producing countries in the world have been tabulated in **Table 1**.

**Table 1: Worldwide Tobacco Production in Metric Tons [4]**

| Rank | Country | Production Quantity (MT) |
|---|---|---|
| 01 | China | 3157000 |
| 02 | Brazil | 951933 |
| 03 | India | 830000 |
| 04 | United States of America | 271363 |
| 05 | Malawi | 174928 |
| 06 | Argentina | 145000 |
| 07 | Indonesia | 130300 |
| 08 | United Republic of Tanzania | 130000 |
| 09 | Zimbabwe | 111570 |
| 10 | Pakistan | 102834 |

**Plant Profile**

Tobacco is a product prepared from leaves of the tobacco plant by curing them. Tobacco consists of dried leaves of '*Nicotiana tobacum*', belonging to the Family '*Solanaceae'*. While more than 70 species of tobacco are known, the chief commercial crop is *Nicotiana tobacum.* The more potent variant *Nicotinum rustica* is also used around the world **(Figure 1)**.

Tobacco contains nicotine as an active ingredient that leads to addiction which is why so many people who use tobacco find it difficult to quit. Tobacco is a plant grown for its leaves which are dried and fermented before being put in tobacco products. There are also many other potentially harmful chemicals found in tobacco or created by burning it **[5]**.

**Climatic Conditions Required for Tobacco Cultivation**

- ✓ Region – Semi Tropical region/Tropical.
- ✓ Temperature – $20^0$C-$30^0$C.
- ✓ Cultivation Period – Annually.
- ✓ Seed Germination Condition – Cold/Early Spring.
- ✓ Germination Time – 07-10 days.
- ✓ Crop Height –01-03 meters.

**Chemical Test for Identification**

Aqueous extract of tobacco when treated with cyanogens bromide solution gives orange color.

**Morphological Characters**

Colour – Green or slightly brown

Odour – Characteristic to nicotine

Taste – Bitter

Size – 62 to 80 cm in length, 30 to 45 cm in width

Shape – Ovate, Elliptic or Lanceolate.

**Chemical Constituents of Tobacco**

Tobacco contains pyridine – piperidine type of alkaloids (0.5-1.5%) among which the most prominent is Nicotine. The other alkaloids are nornicotine and anabasine. **[5]**

**Mechanism behind Tobacco Addiction**

Long term use of tobacco brain changes brought on by continued nicotine exposure it results in addiction when a person tries to quit he or she may have withdrawal symptoms such as-

- ❖ Trouble in sleeping.
- ❖ Problems in paying attention.
- ❖ Irritability.
- ❖ Increased appetite.
- ❖ Powerful cravings for tobacco.

**Tobacco's effect on the Brain**

The Nicotine in any Tobacco product readily absorbs into the blood when person uses it. When entering into the blood, nicotine immediately stimulates the adrenal glands to release the hormone Epinephrine (Adrenaline). Epinephrine stimulates the central nervous system (CNS), increases blood pressure (BP), breathing and heart rates. As with drugs such a Cocaine and Heroin, the brain is activated by nicotine which reward circuits and also increases level of the chemical messenger Dopamine which reinforces rewarding behaviours, Studies suggest that other chemicals in tobacco smoke such as Acetaldehyde, it may enhance nicotine's effects on the Brain **[6] (Figure 3)**.

**Different Ways of Tobacco Consumption**

People can smoke, chew or sniff tobacco. Tobacco smoked products has cigarette, cigars, bidis and kreteks and some other people will smoke loose tobacco in a pipe or hookah it is also called water pipe. Products of chewed tobacco include chewing tobacco, snuff, dip and snus; snuff can also be sniffed.

**Miscellaneous Health Effects of Tobacco Use**

- ➢ Lungs Cancer
- ➢ Chronic Bronchitis
- ➢ Emphysema( enlarge and damaged lungs)
- ➢ Hearts Diseases.
- ➢ Cancers: - Mouth Cancer, Leukemia.
- ➢ Increases the Risk of Miscarriage in pregnant women.
- ➢ Smoking during pregnancy- Premature infants, Abnormal children etc.
- ➢ Pneumonia, Cough.
- ➢ Asthma.
- ➢ Sometimes death from sudden infant death syndrome **[7]**.


**Figure 1: Diagrammatic Representation of Tobacco Plant**

**Figure 2: Cigarette Smoker**


**Figure 3: Brain Images of Chain Smoker and Non Smoker**

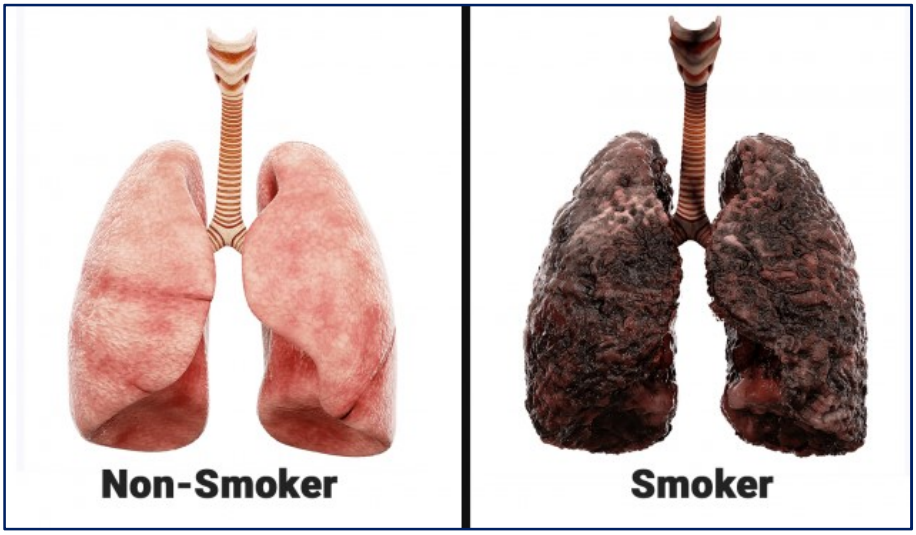



**Figure 4: Image showing Damage to Lungs after Prolong Exposure to Tobacco Smoke**

**Tobacco Mesophyll Cells – Isolation**

A Procedure using a fungal pectinase was developed to rapidly release mesophyll cells from tobacco leaves, 50-90% of the released cells were morphologically intact and were converted into spherical protoplast by cellulose treatment. Cells isolated from tobacco mosaic virus inoculated leaves supported multiplication of the virus during subsequent incubation.

**Tobacco Mesophyll Proto Plasts – Infection**

It was provided at that the protoplasts prepared from mesophyll of *Nicotina tobaccum* are infected by tobacco mosaic virus. The infection occurred when purified tobacco mosaic virus particles were added to a protoplast suspension in the presence of poly –L- ornithine. The virus multiplied in this protoplast to a level of 10 ‘6 virus particles per infected protoplast during 24 hours of incubation. The efficiency of infection was remarkably high exceeding that by mechanical inoculation of tobacco leaves.

Isolated protoplast from healthy tobacco mesophyll tissues were infected by contact with infectious RNA from tobacco mosaic virus (TMV). During subsequent incubation of the protoplasts in a liquid medium, a synchronous multiplication of TMV occurred and the amount of intracellular virus reached a maximum after 22 hrs. Fluorescent antibody staining showed that 2-7% of protoplasts were infected. Average virus yield per infected protoplast was estimated to 0.9-5.5 × $10^5$ particles. **[8]**

**TOBACCO DEPENDENCE**

Tobacco dependence is defined as “Cluster of behavioral, cognitive and physiological phenomenon that develop after repeated tobacco use and that typically include a strong desire to use tobacco, difficulties in controlling its use, persistence in tobacco use despite harmful consequences, a higher priority given to tobacco use than other activities and obligations, increased tolerance and sometimes a physical withdrawal state”.

Nicotine is readily absorbed from the respiratory tract, oral mucosa and skin. There is minimal absorption through the gastro intestinal tract when administered orally. Cigarettes are highly effective mechanism for delivering nicotine. Inhaled nicotine takes about 10-19 second to reach the brain and its stimulation releases chemicals which ensure feelings of goodness, alertness and energy.

The smokers go through this process thousands of time over the course of their smoking careers and this may lead them to identify Cigarettes are effective self-medication, even if the effect is the negative one of withdrawal relief rather than any absolute improvement. As any former smoker will tell you, it takes

months or years achieve the extension of these conditions.

Girls and women are more likely to smoke to control their weight than males. They tend to gain more weight after quitting smoking. Female smokers also derive greater subjective pleasurable effects from nicotine than males who smokes. They are at increased risk for female specific reproductive risk among those who use certain birth control **[8, 9, 10]**.

**Figure 5: Addictive Female Depending on Tobacco Smoke**

As the person stops tobacco use, these chemicals decrease in the body and withdrawal symptoms start. These can be very distressing for the unprepared tobacco user. Thus the tobacco user is compelled to continue using tobacco, hence trapped in the vicious cycle

Studies show that tobacco users must effectively deal with both the physical and psychological symptoms i.e. alteration of the mood.

**TREATMENT**

Both Medication and Behavioral treatment can help to treat the addiction. But, the combination of medication with counseling is more effective.

The Indian government has established a National level tobacco cessation Quitline in Vallabhbhai Patel Chest Institute (VPCI), New Delhi with a toll free number – 1800-112-356 and the services expanded to regional satellite canters since 2018 and counseling is now available in regional languages **[11]**.

**MEDICATION**

**Nicotine Replacement Therapy**

Five medications approved by the US Food and Drug Administration (FDA) deliver nicotine in a form that does not involve the risks of smoking. NRT are used for a short period of time and should ne tapered down to a low dose before stopping. The five NRT medications for smoking cessation are described below **[12, 13]**.

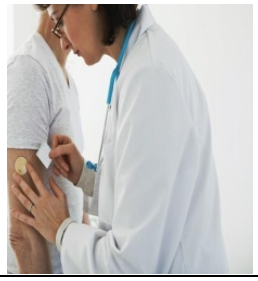
This therapy uses low nicotine products, thereby cutting down on the craving the symptoms of nicotine withdrawal.

**Antidepressant Medicine - Bupropion**

Bupropion blocks neuronal uptake of dopamine and norepinephrine and has antagonist activity on the α4β2 nicotinic receptor. By blocking reuptake, bupropion increases brain levels of dopamine and norepinephrine, simulating effects of nicotine. It is marketed for smoking cessation as a sustained – release preparation. The drug works in both depressed and non-depressed smokers. The usual duration of bupropion treatment is 12 weeks, but extended bupropion therapy for a year reduces relapse and enhance long-term quit rates (105) with lower quit rates it considered to be second line after combination NRT and varenicline.

The main adverse effects of bupropion relate to its nervous system stimulant actions. Some smokers are intolerant to bupropion because of anxiety, agitation, and insomnia. Bupropion reduces the seizure threshold and should not be used in smokers who are at risk for seizures. In overdose, Bupropion causes tachycardia and hypertension but there is no evidence of increased cardiovascular events in smokers with preexisting stable in cardiovascular diseases **(Figure 6) [14]**.

**Table 2: Various formulations for Nicotine Replacement Therapy**

| Nicotine Replacement Therapy | | | | | |
|---|---|---|---|---|---|
| **Medication Form** | **Transdermal Patches** | **Gum** | **Spray** | **Lozenges** | **Inhalers** |
| **Dose Formulation** | **7 mg, 14 mg, 21 mg - (24-hour release)** | **2 mg and 4mg** | **10mg/ml aq. solution** | **2mg and 4mg** | **10mg cartridge delivers 4mg nicotine vapor** |
| **Diagrams** |  |  |  |  |  |

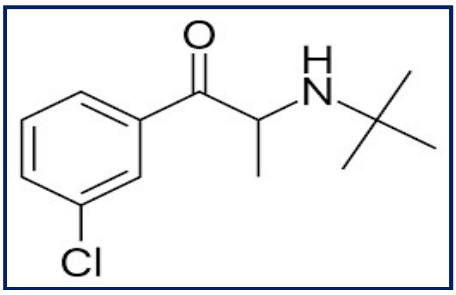



**Figure 6: Structure of Bupropion (Medicine to treat tobacco withdrawal associated depression)**

## Varenicline – Partial Agonist

Varenicline block the ability of nicotine to activate α4β2 receptors and thus to stimulate the central nervous mesolimbic dopamine system. The drug exerts mild agonistic activity at this site, though at a level much lower than nicotine; it is presumed that this activation eases

withdrawal symptoms. It not shows the activity towards other nicotinic receptors, non-nicotinic receptor and transports. The elimination Half life of Varenicline is approximately 24 hours. **[15]**

**Effective in Combination**

Studies have also examined combination of medications to improve efficacy. The combination of nicotine patch (Steady concentration of nicotine over the course of the day).

One study found a combination of bupropion and nicotine patch to be more efficacious that patch only but not bupropion alone. A combination of nortriptyline over nicotine patch alone.

To date, the results suggest that there is no evidence to strongly support combining a nicotine and non-nicotine patch with an ad libitum from of NRT may confer some benefits **[14, 15]**.

**Second Line Tobacco Dependence Cessation Medications**

**Cystine**

It is an alkaloid extracted from the seeds of *Cytisus laburmum* commonly known as the golden chain or golden rain, a common garden plant in central and Southern Europe. Cystine has been used for smoking Cessation in many countries from many years. Cystine like varenicline is a partial agonist. And thus it shows nicotine like effect, while at the same time it desensitized or block the effect of nicotine from the tobacco.

The recommended treatment regimen involves tapering doses over 25 days, a treatment course i.e. shorter than 12 weeks recommended for most other smoking cessation. Cystine have the half life 4.8 hours and it rapidly eliminated from the body.

This drug is well tolerated with the most common side effects, like nausea, dyspepsia, vomiting and dry mouth **[14, 15]**.

**Nortriptyline**

It is a tricyclic antidepressant that blocks the neuronal reuptake of norepinephrine, thereby increasing level of neurotransmitter in the brain. These actions stimulate some of the neurotransmitters in the brain.

**Clonidine**

It is a central alpha-2 adrenergic receptor agonist that reduces symptomatic activity, resulting in the sedation. Benefit of the clonidine, it shows calming effect and it is most useful in smokers with anxiety as a major withdrawal symptom.

**Precision Medicine**

Precision medicine is an emerging approach to treatment. It is based on the personalized treatment. An individual's rate of nicotine metabolism has been proposed as a basis for medication selection. Nicotine metabolism is rapid in the tobacco dependent.

Nicotine is metabolized primarily by the liver enzyme CYP2A6. Cotinine is the primary metabolite, further metabolized to 3'-hydroxycotinine by the same enzyme. The cotinine to hydroxycotinine ratio termed the nicotine metabolite ratio, can be measured in smoker's blood plasma or urine as a biomarker of the rate of nicotine metabolism.

This approach is cost effective remains to be determined and at present there is no widely available clinical test for the nicotine metabolism ratio **[14, 15]**.

**Behavioral Treatments**

Behavioral Treatments use a variety of methods to quit smoking in people it ranging from self-help to counseling.

Traditionally, behavioral approaches were developed and delivered through formal settings, such as smoking cessation clinics and community and public health settings. Over the past decade, however, researchers have been adapting these approaches for mail, telephone and internet formats, which will be more acceptable and accessible to smokers who are trying to be quit. Indian Government give a toll free helpline – 1800-11-2356 **[14, 15]**.

**Intervention**

Intervention aimed as preventing tobacco initiation (starting to smoke on a regular basis) among teenagers. Some Studies shows weak effect on self reported smoking behaviors in answer to the question 'Are you a regular smoker?' the average intervention reduce the percentage of smokers in the week or month preceding the survey by between 3-17%. Some studies finding stronger effects were not included due to methodological bases **[15]**.

**Counseling**

Counseling is the process to guide patients especially by a trained person on a professional basis. To resolve the psychological problems and difficulties.

Counseling involves motivating the tobacco user to quit by examining the consequences from smoking. It also involves educating the tobacco user about the beneficial health effects from smoking Cessation, beneficial effects which experienced even when cessation at an older age.

Problem solving i.e. discussing methods and coping skill these counseling, to deal with high risk situations for Tobacco dependence and obtaining support.

The guidance of the specialist is the major advantage to tobacco dependence. The frequent personal counseling, Telephone quit lines have the major advantage its efficacy, its accessibility and reach to a large population of diverse tobacco dependence **(Figure 7) [16]**.

**Social Media**

Comprehensive advertising and promotion bans on effects of advertising these products. Ban on cigarette advertising and promotion led to significant reductions in

cigarette smoking. Ban on advertising in high income countries could reduce tobacco consumption by more than 4%. Nowadays some advertisements are helpful to prevent the people to become tobacco dependence. They shows or tell 'Tobacco Causes Cancer', 'Tambakhu Jan leva Hai' these kind of some slogans are prepared and make awareness in the society **(Figure 8) [16, 17]**.

**Figure 7: Counseling Effective way to treat tobacco dependence**


**Figure 8: Advertisement Symbol for Social Cause**

## CONCLUSION

In this review, an attempt has been made to summarize all the possible treatments that are available to treat tobacco dependence. It will be useful for making people free from tobacco addiction. In future, more endeavours will be made towards achieving the targets of 'Tobacco Addiction Free World' especially for the youth.

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