INTERNATIONAL JOURNAL OF PHARMACEUTICAL SCIENCES
[ISSN: 0975-4725; CODEN(USA): IJPS00]
Journal Homepage: https://www.ijpsjournal.com

OPEN ACCESS

Review Article

Nicotine Replacement Therapy: A Comprehensive Review on Strategies for Smoking Cessation and Future Perspectives

Dr. Nilesh. S. Mhaske*, Yashwant. S. Deotarse

Dr. Vitthalrao Vikhepatil Foundation's, College of Pharmacy, Vadgaongupta (Viladghat), Post. MIDC, Ahilyanagar.

ARTICLE INFO

Published: 04 Oct 2025

Keywords:
Nicotine Replacement Therapy, Smoking Cessation, Electronic Cigarette, Natural Agents, Prescription Drugs, Pregnancy

DOI:
10.5281/zenodo.17263789

ABSTRACT

Tobacco use is one of the main cause of preventable illness and death around the world. It is linked to serious diseases such as cancer, asthma, heart problems, and lung infections. Nicotine present in tobacco makes people addicted because it gives a feeling of pleasure and relaxation by releasing dopamine in the brain. Quitting tobacco is difficult due to withdrawal symptoms, so Nicotine Replacement Therapy (NRT) helps by giving small and controlled doses of nicotine through products like chewing gums, patches, lozenges, nasal sprays, inhalers, and sublingual tablets. These methods help reduce cravings and make quitting easier. Apart from NRT, medicines such as bupropion, varenicline, nortriptyline, and clonidine are also used to support people in stopping smoking. New vaccines like NicVax and TA-NIC are under study for future use. Electronic Nicotine Delivery Systems (ENDS), such as e-cigarettes, may reduce harmful chemical exposure but their long-term safety is still uncertain. Natural remedies like fresh lime, black pepper, St. John's Wort, and calamus have also shown positive effects in helping people quit smoking. During pregnancy, NRT may slightly increase the chances of quitting but should be used carefully. Overall, NRT and related therapies play an important role in helping smokers overcome nicotine addiction and improve their overall health.

INTRODUCTION

Before we focus on nicotine replacement therapy, we should know about what nicotine is and what it does, after someone consumes it. Nicotine is a natural component of tobacco specifically, in Species like *Nicotiana tabacum*, having a chemical structure in which two nitrogen containing rings are interconnected i.e., a pyridine ring and a pyrollidine ring with one methyl group [22]. This nicotine strengthen a person's behaviour

***Corresponding Author:** Dr. Nilesh. S. Mhaske
Address: *Dr. Vitthalrao Vikhepatil Foundation's, College of Pharmacy, Vadgaongupta (Viladghat), Post. MIDC, Ahilyanagar.*
Email ✉: nilesh.2273@gmail.com

Relevant conflicts of interest/financial disclosures: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

towards tobacco and cigarette addiction [1,2,3].While, tobacco and cigarette are the most common forms of nicotine consumption. The other components of tobacco cause wide spread mortality [1,2,3,4]. The use of nicotine containing products potentially increases the chance of developing several infectious disease and Deadly health problems like cancer, heart disease and lung diseases such as, tuberculosis [23]. As nicotine is a ‘‘psychoactive ’’ chemical compound, when consumed by an individual, it cause the release of dopamine hormone in the body that create a feeling of improved mood and satisfaction [22].But here is an interesting fact that, the nicotine is not naturally produce in the human body [22]. That’s why, individuals specifically, adults consumes nicotine from tobacco containing substances like, cigarette and smokeless tobacco. Hence, nicotine is a principal modulator of psychopharmacological effect associated with its addiction [5].The possible developing hazard of nicotine and nicotine containing products can greatly decreased, when the addicted person decided to quit, but it is found difficult due to potent addiction to the nicotine containing products. Henceforth, Nicotine Replacement Therapy (NRT) comes into existence. Nicotine replacement therapy has the aim to reduce the motivation to consume nicotine-containing products and ultimately reduce the nicotine withdrawal symptoms through the alternate delivery of nicotine [6]. There is evidence that, many clinical guidelines recommended nicotine replacement therapy as a first line treatment for the individuals looking for pharmacological help with smoking cessation [7].This review article aims to summarize the currently available forms of nicotine replacement therapy (NRT), And the role of nicotine replacement therapy for smoking cessation, along with the use of prescription drugs for smoking cessation, electronic nicotine delivery system, and the efficacy of natural agents in smoking termination including, effect of NRT on pregnancy.

Currently Available Forms of Nicotine Replacement Therapy:

1.Nicotine Chewing gum (Nicotine Polacrilex)

Nicotine Chewing gum was the first form of nicotine replacement therapy (NRT).Which is made available to Consumers [14].Nicotine chewing gum can be purchased without an prescription [24].Nicotine chewing gum is a rapid acting form of nicotine replacement therapy (NRT).Nicotine is taken in through the lining of the mouth [24].Chewing gum are available in both 2 mg and 4 mg dosage form [13].Acidic beverage’s like Soda, Beer and Coffee can interfere with the buccal absorption of nicotine. Therefore, individual should avoid such acidic beverages for 15 minutes before chewing the nicotine gum [14]. Possible side effects includes, stomach and jaw discomfort are usually caused by improper use of nicotine gum. Chewing the gum too fast or swallowing the nicotine, the nicotine gum may also can damage the dental work [24].

2.Nicotine Lozenges

Nicotine lozenges can also be purchased without a prescription. These lozenges are available in two strengths i.e.,1 mg and 2 mg [24]. The nicotine lozenges provide an alternative for individuals who need control nicotine strength and do not finding chewing gum acceptable. The amount of nicotine absorbed from lozenges seems higher than the amount of nicotine absorbed from nicotine chewing gum [15]. Possible side effects, if you experience sleep related problems when using nicotine lozenges, then avoid their use prior to sleep.

3.Nicotine Sublingual Tablets

Nicotine sublingual tablets are designed to be kept under the tongue, and the nicotine present in the tablet is absorbed sublingually, similar to the nicotine lozenges. The nicotine sublingual tablet poses the advantage of not require chewing unlike the nicotine chewing gum. The concentration level of nicotine obtained via nicotine sublingual tablets and nicotine lozenges are comparable [16]. It is recommended that, individual utilize this product for a minimum of 12 weeks. Following the initial 12 week period, reduction in number of tablet consumed may be considered [9].Side effects may results in, the patient may experience irritation in the oral cavity and the throat.

4. Nicotine Oral Inhalers

The nicotine oral inhaler was designed to satisfy the ''hand to mouth ritual.'' This type of nicotine delivery reduces physiological tobacco withdrawal symptoms. It is important to note that, the nicotine oral inhaler appears to deliver the majority of nicotine to the oral cavity with a minimal amount of nicotine delivered to the lungs. Nicotine oral inhalers can purchased only through prescription[24]. A cartridge of nicotine oral inhaler consist of 10 mg of nicotine [17].Certain adverse effects including, elevated heart rate which may arise from excessive nicotine consumption. Nicotine withdrawal symptoms may manifest, if the nicotine replacement therapy (NRT) dosage is insufficient [24].

5.Nicotine Nasal Spray

Nicotine nasal spray are only available by the prescription [24]. Nicotine nasal spray are designed to deliver nicotine more quickly, as the nasal spray absorbed in to the blood more quickly as compared to all other forms of nicotine replacement therapy [18]. Single doses of nasal spray Per hour (10mg nicotine) for 10 hours produce an average Concentration of up to 8ng/ml [9]. Individual with a history of Asthma, allergy And nasal polyps or sinus related condition may be advised by their healthcare provider to consider an alternative form of nicotine replacement therapy [24].

Safety Note: This form of nicotine replacement therapy present a more serious risk to small children and pets as, the empty bottles of nasal spray contain sufficient nicotine to cause health harm [24].

6.Nicotine Transdermal Patch

Nicotine transdermal patch can be purchased without prescription. This transdermal patches are available in the strengths of 5mg, 7 mg, 10 mg, 14 mg, 15 mg and 21 mg [8,9,17]. Usually, highly dependent smoker should use a high dose patch, and less dependent smoker use a low-dose patch. Current evidence bears on the safety of long lasting use of nicotine patch treatment for tobacco sobriety [12]. The patient simply applies the patch to the body in the morning rather than, actively using a product throughout the day. Nicotine patches are available in different strengths, and can deliver nicotine between 5mg and 21 mg over 24 hour period resulting in a plasma level similar to those observed in heavy smokers [8].Possible side effect may includes, local skin irritation.

Various NRT Forms and Their Direction of Use:

Table no: 1

Sr.no	NRT form [11,23].	Available Dose [23].	Direction Of Use [11,14,23,24].	Adverse effect [23].	Available Marketed Formulations [22].

1.	Chewing gum	2mg, 4mg	Until the test becomes strong, chew the gum. Then park the gum between cheeks and gum. Chew again if, required.	Hiccups, Jaw ache, Mouth soreness	Nicotex nicotine chewing gum, Nicorette chewing gum
2.	Nicotine lozenges	2mg, 4mg	Allow to dissolve in mouth by time to time. For about 20 to 30 minutes.	Heartburn, Nausea	NOSMOK, Snicks, NiQuitin
3.	Nicotine sublingual tablets	2mg, 4mg	Tablet is allowed to rest under tounge until dissolves.	Mouth soreness	Nicorette micro tabs
4.	Nicotine transdermal patches	5mg, 7mg, 10mg, 15mg,21mg	Applied on clean, unbroken skin.	Local skin irritation, Insomnia	Nioderm transdermal patch
5.	Nicotine oral inhaler	10 mg per cartridge	Spray directly in mouth, avoiding lips.	Local mouth irritation	Nicorette oral inhaler, Nicontrol oral inhaler
6.	Nicotine nasal spray	0.5 mg per spray	Take schematic puffs about every 2 seconds for 3 minutes	Nasal irritation	CigStop nasal spray, Nicorette nasal spray

Approved Drugs for Nicotine Replacement Therapy

1. Bupropion

Bupropion is an antidepressant drug but, also inhibit the re-uptake of nor-adrenaline and serotonin in the central nervous system[25,26]. Cigarette smoking leads to nicotine enters into the blood circulation and penetrating the blood brain barrier (BBB) as a result, dopamine is released.Bupropion is believed to work primarily by preventing the re-uptake of dopamine most likely through the dopamine transporter system [33]. Bupropion is a prescription drug, bupropion-Sr, is a tablet comes in one dosing strength 150 milligram. Bupropion include side effects such as, Insomnia, Dry mouth, Nausea and Headache. [24].

2.Varenicline

Varenicline is a key pharmacotherapatic agent which is used for smoking cessation. Certain studies have shown that varenicline is better than bupropion and it is equally effective as nicotine replacement therapy. Varenicline helps to lower nicotine withdrawal symptoms as compared to other medications [27]. Varenициclines ability to bind specifically to a4B2 and nACh receptor as a partial agonist, inhibit the binding of nicotine to these receptors hence, it had success in aiding smoking cessation.

Due to partial agonism of Varenicline, it significantly reduces activation of mesolimbic dopamine pathway linked to nicotine addiction [28,29]. The frequent side effect of varenicline include, Headache, Nausea, Sleeplessness, Constipation, Sleep walking and Disturbed sleep. Steven-Johnson syndrome have all been linked to varenicline. The patient receiving varenicline treatment should also be monitored for any abdominal pancreatitis. As, this medication may raise the risk of pancreatitis [30,31].

3.Nortriptyline

Nortriptyline is an anti-depression medication that aids in the reduction of tobacco withdrawal symptoms. Studies have indicated that, it increases the probability of successful ceasing smoking when compare to individual who do not take medication. Nortriptyline is typically initiated 10 to 28 days prior to the designated quit date to permit it to attain a stable concentration within the body. This medication may affect your ability to operate a vehicle or machinery and certain other medication are contraindicated for concomitant use. The dosage of nortriptyline must be reduced gradually, abrupt cessation of the medication may result in serious adverse effects. Individuals with cardiac condition should exercise caution when using this medication, it is imperative to inform all Healthcare provider of current nortriptyline usage [24].

4.Clonidine

Clonidine represents an additional pharmacological intervention that has been investigated for its potential to assist individuals in smoking cessation. While it’s utilisation is not wide spread. It may serve as a viable alternative for patients in instances where, the nicotine replacement therapy and other prescription medication prove ineffective. Prior to commencing treatment with this medication, it is imperative that, both your health care provider and pharmacist poses comprehensive knowledge of your current medication regimen. Common side effects include constipation, Dizziness, Dry mouth, Weakness. The medication can also affect your ability to drive or operate machinery. The cessation of this medication should not be a abrupt.

The dosage must be reduce gradually over the several days to mitigate the potential for Tremor’s, Confusion, Agitation or Rapid elevation in blood pressure [24].

Nicotine Replacement Modalities Under Trial:

Table no: 2

Sr. no	Vaccine [23].	Sponsor [23,24].	Clinical trial phase	Results [21,33].
1.	NicVax (Bacterial exoprotein conjugate vaccine)	Nabi Biopharmaceuticals	Phase III	Multiple studies have shown that, higher dose and high antibody responders generally achieve better smoking cessation outcomes. There was no any statistical difference between NIC VAX and placebo group.

2.	TA-NIC (Recombinant cholera toxin-B subunit carrier)	Celtic pharma	Early phase I	Shows potential efficacy but, there is requirement of more comprehensive research to validated these findings.
3.	NICCINE (Tetanus toxoid conjugate)	Independent pharmaceutical AB	Phase II	Shows high safety and immunogenicity. Initial studies have shown short term increase in abstinence rates.
4.	Nic-Qb	Novartis	Assessed in phase I, phase IIa, Phase IIb	Long term efficacy varied and not uniformly significant across all participant's.

Further investigations are required to optimise these vaccine and completely understand their potential for smoking cessation strategies [32].

Electronic Nicotine Delivery System (ENDS) :

Electronic nicotine delivery system (ENDS) include electronic cigarettes, consist of heated tobacco product which often referred as HTP's. Electronic cigarette are affordable, portable and self powered devices. This devices consist of nicotine without any combustion. Electronic cigarette are available in wide range of Size, Flavor, Shape and Performance level. The electronic cigarette liquid usually consist of water, glycerol, propylene glycol and different types of flavourings. Currently available electronic cigarette in the market contains nicotine salt formulations that have a smoother taste as compared to conventional cigarettes. And the cigarette are less irritating and improve overall sensory experience of vaping. Bioavailability of nicotine does not totally depend upon the electronic cigarette device, but also it depends upon the technique and experience of the user. Regarding to the use of electronic nicotine delivery system, the combustion is absent [34]. This combustion is responsible for most of the toxic substances inhaled with cigarette smoking. Many studies have demonstrated that the concentration of toxicants present in electronic cigarette, is significantly lower than the concentration present in traditional cigarette [35].

There are several case reports associated with acute lung damage associated with the use of electronic cigarettes [36]. Furthermore , the utilisation of electronic cigarette may elevate incidence of wheezing and exacerbation as well as deficiency in respiratory function among individuals afflicted with chronic obstructive pulmonary disease (COPD) and asthma [36,37,39]. On other hand, the studies have reported that transition from cigarette smoking to exclusive electronic cigarette use may reduce the frequency of exacerbation in individuals who would have otherwise continue to smoke [40].

Use of ENDS is associated with oxidative stress and endothelial damage, and nicotine itself has a known stimulant effect on blood pressure and heart rate. However, the cardiovascular effect of electronic cigarette may be less than those of tobacco cigarettes [41]. Switching from traditional smoking to vaping, may reduce second hand exposure to nicotine. But, it does not completely eliminate exposure to noxious substances [42]. The role of electronic cigarette as an aid in smoking cessation in real world scenario remain a debated topic. Certain studies demonstrate the advantage of electronic cigarette while other do not [43,44].

Intervention On Natural Agents In Smoking Cessation:

Several methods have been developed to assist in smoking cessation. However, Limited information is available regarding the association with utilisation of natural agent in this process. The role of natural agent in smoking cessation should not be disregarded, as they play an significant role. The medical application of natural agent is substantial. A negligible amount of research has been conducted on the role of natural agent in smoking cessation. Following are certain natural agents which helps in smoking cessation.

1.Fresh lime

Lime is radially accessible and may be utilised as an alternative to nicotine chewing gum in smoking cessation. Researchers from srinakharinwirot university in thailand, conducted randomise control trial to determine the efficacy of fresh lime in smoking cessation as compared to nicotine chewing gum. The study has demonstrated that, the lime can be effectively used as a smoking cessation agent .Furthermore, lime possess anti microbial activity against multiple strains of e.coli, and smoker typically exhibit compromised immunity [46,47,48].

2.St. John wort

St. John wort is an herb which contain active ingredients like, phoroglucinol derivatives, naphthodianthrones and flavonoids. Also it act as an anti- depressant and it also effective in smoking cessation [50]. The extracts of St. John wort basically Works by inhibiting the re-uptake of serotonin (5HT) and norepinephrine into pre-synaptic axon.

Certain study are also demonstrated that, the St. John wort herb is not effective in smoking cessation. [51].

3.Black pepper

The effectiveness of black paper as an aid in smoking session has been substantiated by various studies worldwide. A study conducted by Jed E. Rose, involving 48 participants demonstrated that craving for cigarette where significantly reduce in responders who inhale black paper essential oil vapours, this intervention significantly reduce cravings for duration for about 3 hours [49].Black paper product stimulate the sensory experience of smoking which may provide short term satisfaction and elevate cravings for cigarette smoking in individuals with nicotine dependence.

4.Calamus

Calamus is used in the treatment of chest pain, problems related to appetite, indigestion, fever and cough. Several active constituents and essential oils are isolated from calamus. Calamus is potent antioxidant, antibacterial and effective anti-depressant agent.

According to certain studies, it has effective role in smoking cessation. The exact mechanism of calamus in smoking cessation is not known as the previous clinical trial have been done. Hence, there is requirement to conduct more clinical trials and research on the role of calamus in smoking cessation [52].

Effect Of Nicotine Replacement Therapy On Pregnancy :

Pregnant women are susceptible to adverse effect which may also result in potential negative consequences for the child. This consequences encompass low birth weight, preterm birth, restricted head growth, placental issues and an elevated risk of stillbirth or miscarriage. Additionally, there is evidence of development consequences for children who wear exposed to smoke prenatally including poor lung functions and visual impairment [53]. In a systemic review that assessed pharmacological interventions during pregnancy, it was found that, nicotine replacement therapy(NRT) during pregnancy, increase smoking cessation rate by approximately 40% in late pregnancy. However, when a partial studies are excluded its effectiveness is no greater than that of a placebo group. It is not established that NRT affect birth outcomes either positively or negatively [55] . Dosing and the adverse reaction profile should be considered along side other risk benefit factor, when determining weather pharmacotherapy should be used to assist with smoking cessation in someone who is pregnant [55]. The drug varenicline has been evaluated for safety and efficacy during pregnancy. However, the trials were small and while there was no demonstrated teratogenicity. The data are limited [54]. Similarly, there is limited data regarding to the use of bupropion during pregnancy in individuals who are specifically, breastfeeding. There is no published information indicating that, whether the varenicline and bupropion are found in breast milk in amounts that are considered to be harmful for that child or foetus. Varenicline bupropion however, found in breast milk in amount which is not considered to be harmful. Nevertheless, the use of this substances should be avoided unless further evidence becomes available [54].

CONCLUSION:

Tobacco use continues to pose major health risks, making effective smoking cessation strategies essential. Nicotine replacement therapy (NRT) including transdermal patches, chewing gum, lozenges, oral inhaler, nasal sprays, sublingual tablets can increase quit rate by 50 to 70%. Prescription medication such as varenicline, bupropion, codeine, nortriptyline. are also valuable but, require proper understanding of their mechanism, safety especially during the pregnancy. Novel approaches including, electronic nicotine delivery system(ENDS) may reduce exposure to harmful chemicals when use as a complete substitute for cigarette, however, strict regulatory oversite by authorities like FDA is necessary. Natural agents represent an inexpensive and promising adjunct to smoking cessation, through more research is needed to fully evaluate their effectiveness and safety.

ACKNOWLEDGEMENT:

The authors sincerely express their gratitude to Dr. Nilesh S. Mhaske for their valuable guidance, encouragement, and continuous support throughout the preparation of this review article on Nicotine Replacement Therapy. His insightful suggestions and expert supervision have been instrumental in shaping the quality and depth of this work. The author also extend their appreciation to their institution and colleagues for providing the necessary resources and academic environment that facilitated this study.

Conflict of interest :

The author declared no conflict of interest with respect to the authorship and publication of this article.

Availability of data and material :

All the data used in our article are available from publically accessible sources such as PubMed, Elsevier, Wikipedia, etc.

Funding:

The authors received no financial support for the authorship and for publication of this article.

REFERENCE

1. Balfour DJ : The neurobiology of tobacco dependence: a preclinical perspective on the role of the dopamine projections to the nucleus accumbens. Nicotine Tob Res 2004;6:899-912.
2. Garret BE, Rose CA, Henningfield JE : Tobacco addiction and pharmacological interventions. Expert Opin Pharmacother 2001;10:1545-1555.
3. Benowitz NL : Pharmacology of nicotine: addiction, smoking-induced disease and therapeutics. Annu Rev PharmacolToxicol 2009;49:57-71.
4. Balfour DJ : The neurobiology of tobacco dependence: a preclinical perspective on the role of the dopamine projections to the nucleus accumbens. Nicotine Tob Res 2004;6:899-912.
5. Atlanta (GA) : Centres For Disease Control And Prevention (US);2010 ; Available From : http://www.ncbi.nih.gov/books/NBK53018/
6. Silagy C, Lancaster T, Stead L, Mant D, Fowler G : Nicotine replacement therapy for smoking cessation. Cochrane Database Syst Rev 2008;1:CD000146.
7. Le Foll B, Melihan Cheinin P, Rostoker G, Largue G: Smoking cessation guidelines : evidence-based recommendations of French health products safety agency. European Psychiatry 2005;20:431-4.
8. Yildiz D : Nicotine its metabolism and an overview of its biological effects. Toxicon 2004;11:781-3.
9. Henningfield JE, Fant RV, Buchhalter AR, Stitzer ML: Pharmacotherapy for nicotine dependence. Ca Cancer J Clin 2005;5:281-99.
10. Sweeney CT, Fant RV, Fagerstrom KO, Mc Govern JF, Henningfield JE : Combination nicotine replacement therapy for smoking cessation : rationale, efficacy and tolerability. CNS Drugs 2001;15:453-67.
11. Fagerstrom KO : Combined use of nicotine replacement products. Health Values 1994;18:15-20.
12. Prochaska JJ : Nicotine Replacement Therapy as a maintanace treatment. JAMA 2015;7:718-9
13. Hajek P, Stead LF, Aversive smoking for smoking cessation. Cochrane Database Syst Rev 2000;2:CD000546.
14. Shiffman S, Rolf CN, Hellebusch SJ, Gorsline J, Gorodetzky CW, Chiang YKet al : Real world efficacy of prescription and over the counter nicotine replacement therapy. Addiction 2002;97:505-16.
15. Henningfield JE : Nicotine medications for smoking cessation. N Engl J Med 1995;18:1196-203.
16. Molander L, Lunell E : Pharmacokinetic investigation of a nicotine sublingual tablet. Eur J ClinPharmacol 2001 jan-feb;5:635-44.
17. Clinical practice guideline treating tobacco use and dependence. A U.S Public health service report. Am J Prev Med2008 aug;2:158-76.
18. Henningfield JE : Nicotine medications for smoking cessation. N Engl J Med 1995 nov;18:1196-203.
19. Harmey D, Griffin PR, Kenny PJ : Development of novel pharmacotherapeutics for tobacco dependence : progress and future directions. Nicotine Tob Res 2012;11:1300-18.
20. Hartmann-Boyce J, Cahill K, Hatsukami D, Cornuz J:Nicotine vaccine for smoking cessation. Cochrane Database Syst Rev 2012;8:CD097072.
21. Nabi Biopharmaceuticals Announces Results Of Second NicVax (R) phase ||| Clinical Trial

Available From : http://globenewswire.com/newsrelease/2011/11/07/460749/237357/en/nabi-Biopharmaceuticals-AnnouncesResultsofsecondNiVaxRPhase|||ClinicalTrialHtml.
22. Google From : www.google.com.
23. Umesh Wadgave, Nagesh L: Nicotine Replacement Therapy: An overview. International Journal Of Health Sciences, Qassim University 2016;3:426-31.
24. American Cancer Society From : https://www.cancer.org.
25. Smith RF : Animal models of periadolescent substance abuse. Nurotoxicol Teratol 2003;25:291-301.
26. Roddy E : Bupropion and other non-nicotine pharmacotherapies. BMJ 2004;328:509-511.
27. Mc Carthy DE, Versella MV :Quitting failure and success with and without using medication : latent clasess of abstinence and adherence to nicotine monotherapy, combination therapy, and varenicline. Nicotine Tob Res 2019;21:1488-1495.
28. Foulds J : The neurobiological basis for partial agonist treatment of nicotine dependence: Varenicline. Int J Clin Pract 2096;60:571-576.
29. Rollema H, Hurst RS : The combination of agonist and Hurst RS: The combination of agonist and antagonist activities of a4B2 and nAChR ligands to smoking cessation efficacy: a quantitative analysis of litrature data. Psychopharmacol (Berl) 2018;235:2479-2505.
30. Gelfand EV, Cannon CP : Rimonabant : a cannabinoid receptor type 1 blocker for management of multiple cardiometabolic risk factors. J Am Coll Cardiol 2006;47:1919-1926.
31. Cohen C, Perrault G, Soubrie P : Nicotine-associated cues maintain nicotine seeking behavior in rats several weeks after nicotine withdrawal: reversal by the cannabinoid (CB1).receptor antagonist, rimonabant(SR141716). Neuropsychopharmacol 2005;30:145-155.
32. Mooney ME, Sofugolu M : Bupropion for the treatment of nicotine withdrawal and craving. Expert Rev Neurother 2006;6:965-981.
33. Scendoni R, Bury E, Ribeiro ILA, Camerirere R, Cingolani M: Vaccines as preventive tool for substance use disorder: a systematic review including meta analysis on nicotine vaccines, immunogenicity. Hum Vaccine Immunother 2022;18:2140552.
34. Nishant Patidar, Archana M Navle, Nitesh Parsaila, Dinesh Sharma, Prachi Nahar, Sagar Shinde, Nilay Solanki, Ajay Shelke : Nicotine replacement therapy: insights into the mechanisms and potential of nicotine receptor pathway. Am J Transl Res 2025;4:2369-2410.
35. Maloney S, Eversole A, Crabtree M, et al : Acute effects of JUUL and IQOS in cigarette smokers. Tob Control 2021;30:449-52.
36. Miller CR, Schneller Nijam LM, Leigh NJ, Agar T, Quah AC, Cummings KM, Fong GT, O'Connor RJ, Goniewicz ML : Biomarkers of exposure to nicotine and selected toxicants in individuals who use alternative tobbaco products sold in japan and Canada from 2018-2019. Cancer Epidemiol Biomarkers Prev 2025;2:298-307.
37. Wills TA, Soneji SS, Choi K, et al: E-Cigarettes aerosols : a review and risk assessment of selected compounds. J Appl Toxicol 2025;3:364-386.
38. Joshi D, Duong M, Kirkland S, Raina P : Impact of elctronic cigarette ever use on lung function in adults aged 45-85: a cross-sectional analysis ftom the Candidian Longitudinal Study On Aging. bmj open 2021;10:e051519.
39. Allbright K, Villandre J, Crotty Alexander LE, Zhang M, Benam KH, Evankovich J, Konigshoff M, Chandra D : The paradox of the safer cigarette: understanding the pulmonary

effects of elctronic cigarettes. Eur Respir J 2024;6:2301494.https:// doi. Org/10.1183/13993003.01494-2023.
40. Song C, Hao X, Critselis E, Panagiotakos D: The impact of elctronic cigarette use on pulmonary disease: a systematic review and mata analysis. Respir Med 2025;239:107985.
41. Qureshi MA, Vernooij RMW, LA Rosa GRM, Palosa R, O'Leary R: Respiratory health effects of E-Cigarettes : a systematic review. Harm Product 2023;1:143.https:// doi. Org/10.1186/s12954-023-00877-9.
42. Benowitz NL, Liakoni E : Tobacco use disorder and cardiovascular health: Addiction 2022;4: 1128-38.
43. Tattan-Birch H, Brown J, Jackson SE, Jarvis MJ, Shabab L: Secondhand nicotine absorption ftom E-cigarettes vapor vs tobbaco smoke in children. JAMA Netw Open 2024;7:e2421246.
44. McNeill A, Simonavicius E, Brose L, Taylor E, East K, Zuikova E, et al : Nicotine vaping in England: an evidence update including health risks and perceptions 2022;.Available From : https:// assest. Publishing. Service. gov.uk /government/uploads/system/uploads/attachment_data/file/1107701/Nicotine-vaping-in-england-2022-report.pdf.
45. Chen R, Pierce JP, Leas EC, Benmarhnia T, Strong DR, White MM, Stone M, Triland DR, McMe namin SB, Messer K : Effectiveness of E-Cigarettes as aids for smoking cessation : evidence from the PATH Study cohort. Tob Control 2023;e2:e145-152.
46. Jean-Guillaume Starnini, Giulio Natalello, Federico Nigroli, Chiara Diana, Elena Bargagli, Andrea sisto Melani : Electronic Nicotine Delivery Systems (ENDS) : Implications for the clinician 2025;Plum Ther. https:// doi. Org/10.1007/s41030-025-00305-2.
47. Rungruanghriranya MS, Ekpanyaskul MC, Sakulisariyaporn C, Watcharanat P, Akkalakulawas K: Efficacy of fresh lime for smoking cessation. J Med Assoc Thai 2012;95:76-82.
48. Rahman S, Parvez AK, Islam R, Khan MH : Antibacterial activity of natural species on multiple drug resistant Escheria coli isolated from drinking water, Bangladesh. Annal Clinic Microbiol Antimicrob 2011;10:10.
49. Rose JE, Beham FM, Inhalation of vapor from black pepper extract reduces smoking withdrawal symptoms. Drug Alcohol Depend 1996 ;38:257-229.
50. Lawvere S, Mahoney MC, Cummings KM, Kepner JL, Hyland A, Lawrence DD et al : A phase-II study of st. John's wort for smoking cessation. Complem Tharp Medi 2006;14:175-184.
51. Sood A, Ebbert JO, Prasad K, Croghan IT, Bauer B, Schroeder DR : A randomized clinical trial of St. John' wort for smoking cessation. J Alter Complem Medi 2010; 16:761-767.
52. Yaranell E, Abascal K: Botanical remedies for nicotine addiction. Altern complemen Therap 2001;7:337-340.
53. National Institute on Drug Abuse : What are the risks of smoking during pregnancy, North Bethesda : National institute on Drug Abuse From : https:// nida. Gov/publications/reaserch-reports/tobacco-nicotine-e-cigarettes/what are risks-smoking-during-pregnancy.
54. American College of Obstetricians and Gynecologists : Tobacco and nicotine cessation during pregnancy. ACOG Committee Opinion No. 820.Obset Gynecol. 2020;5:e118-e129.
55. Coleman T, Chamberlain C, Davey MA, Cooper SE, Leonardi-Bee J : Pharmacological interventions for promoting smoking cessation

during pregnancy. Cochrane Database Syst Rev 2015;12: CD 019978.

HOW TO CITE: Dr. Nilesh. S. Mhaske*, Yashwant. S. Nicotine Replacement Therapy: A Comprehensive Review on Strategies for Smoking Cessation and Future Perspectives, Int. J. of Pharm. Sci., 2025, Vol 3, Issue 10, 338-349 https://doi.org/10.5281/zenodo.17263789