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Nicotine: therapeutic potential beyond its addictive effect (Mini review)

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Abstract: This mini-review traces the historical and botanical origins of nicotine, describes its chemical structure, stereochemistry (including the (R)- and (S)-nicotine enantiomers), and its primary physicochemical properties. It provides an essential basis for understanding the molecule's pharmacological behavior. Then explores the main routes of chemical synthesis of nicotine, with a particular emphasis on enantioselective approaches leading to the R and S isomers. It also describes extraction techniques, particularly steam distillation, and briefly discusses some nicotine derivatives of pharmacological interest. Finally examines the dual nature of nicotine. On the one hand, its addictive power is explained by its action on the brain's dopaminergic circuits. On the other hand, its neuroprotective, anti-inflammatory and modulatory effects on neurotransmissions make nicotine a promising molecule in the treatment of neurological, psychiatric and inflammatory pathologies.

Keywords: *Nicotine; alkaloids; Nicotiana tabacum plant; receptors; physicochemical properties.*

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1. Introduction

Nicotine is an alkaloid naturally present in the *Nicotiana tabacum* plant, introduced to France in the 16th century by Jean Nicot, from whom it takes its name, and whose structure was discovered by a French chemist Louis Nicolas Vauquelin in 1809. With the chemical formula $C_{10}H_{14}N_2$, nicotine has a particular chemical architecture comprising two heteroaromatic rings: a pyridine ring and a pyrrolidine ring. This structure confers the molecule remarkable physicochemical and pharmacological properties, enabling it to interact selectively with nicotinic acetylcholine receptors in the nervous system. Long considered exclusively a substance responsible for tobacco addiction, nicotine is now the subject of growing scientific interest, particularly due to its therapeutic potential in several medical fields. This dynamic is

well illustrated by the exponential growth in the number of scientific publications on nicotine (>86,000) since 1831, with the first paper added by Scopus to more than 3600 articles over the last five years, reflecting the importance of this field economically and health-wise (**Figure 1a**). The importance of the bibliometric analysis using databases such as Scopus, Web of Science, … was broadly discussed to orient and quantify the scientific level of authors, laboratories, Universities and the possible collaborations (Sahar *et al.*, 2025; Hammouti *et al.*, 2025; Laita *et al.*, 2024; Nandiyanto *et al.*, 2024; Cucari *et al.*, 2023; Knapp *et al.*, 2002). The United States stands out as the leading research power on the subject, producing the majority of published work (**Figure 1b**). In terms of application areas, medicine, pharmacology, and biochemistry appear to be the most active and promising fields for exploring the effects of nicotine, as the percentage of articles in these fields exceeds 90%, as shown in **Figure 2**.

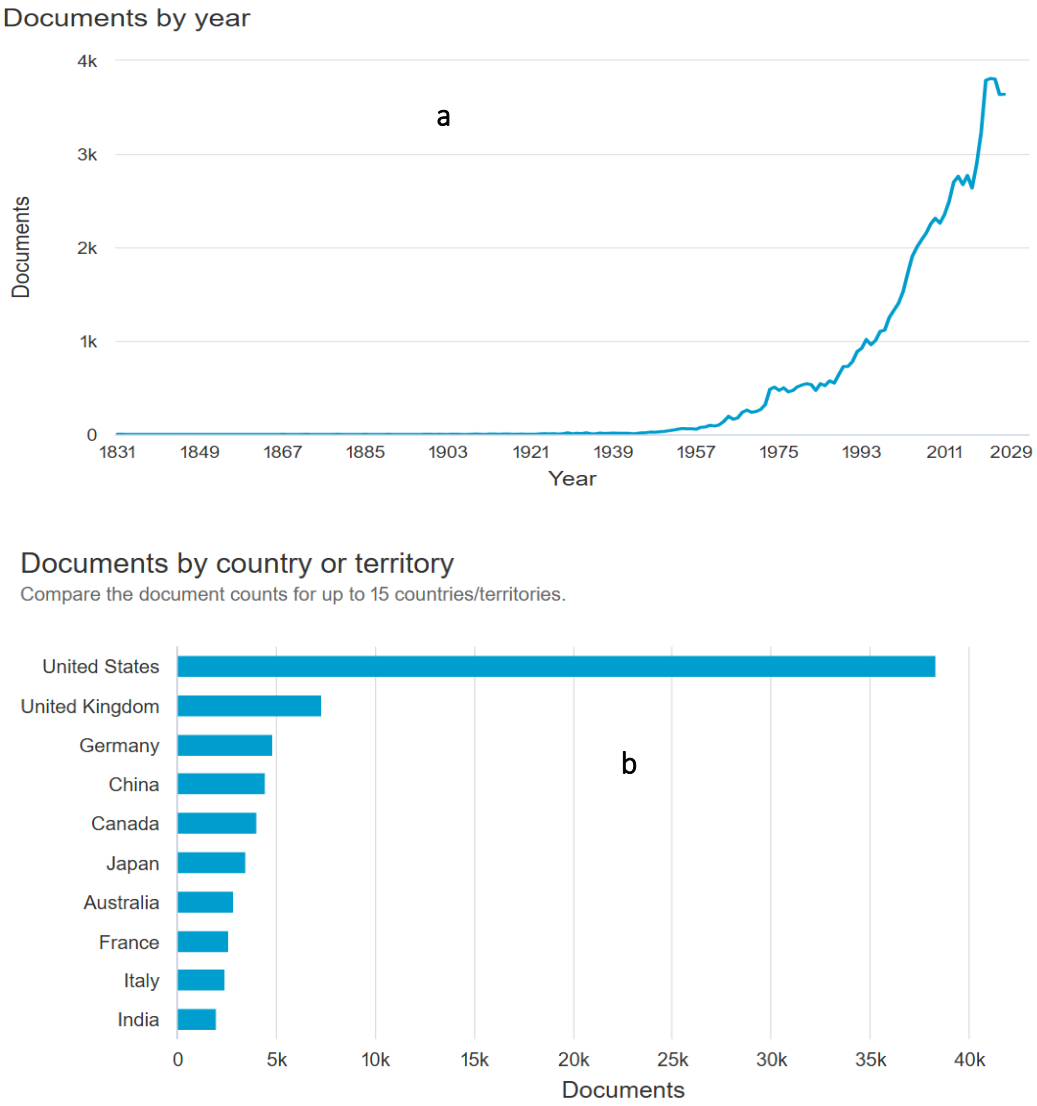

Figure 1: Evolution of the number of scientific publications devoted to nicotine **(a)** and geographical distribution of the top countries **(b)** contributing to research (1831-2024).

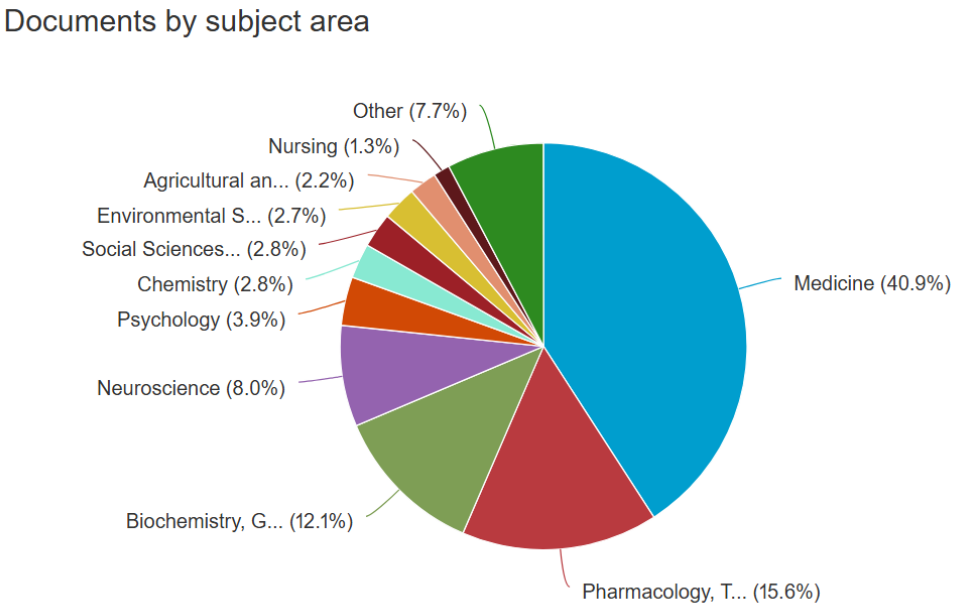

Figure 2: Areas of application of nicotine.

Figure 3 provides the ten most profiler authors collected from Scopus. The first position is presented by "No Author ID found" to indicate that is for the editorial or not personal as association/group… The most published author is the American Benowitz N.L. (UCSF School of Medicine, San Francisco) who contributed by 492 articles on Nicotine and a total of 910 articles, H= 130 and > 69,000 citations by more than 41,470 documents.

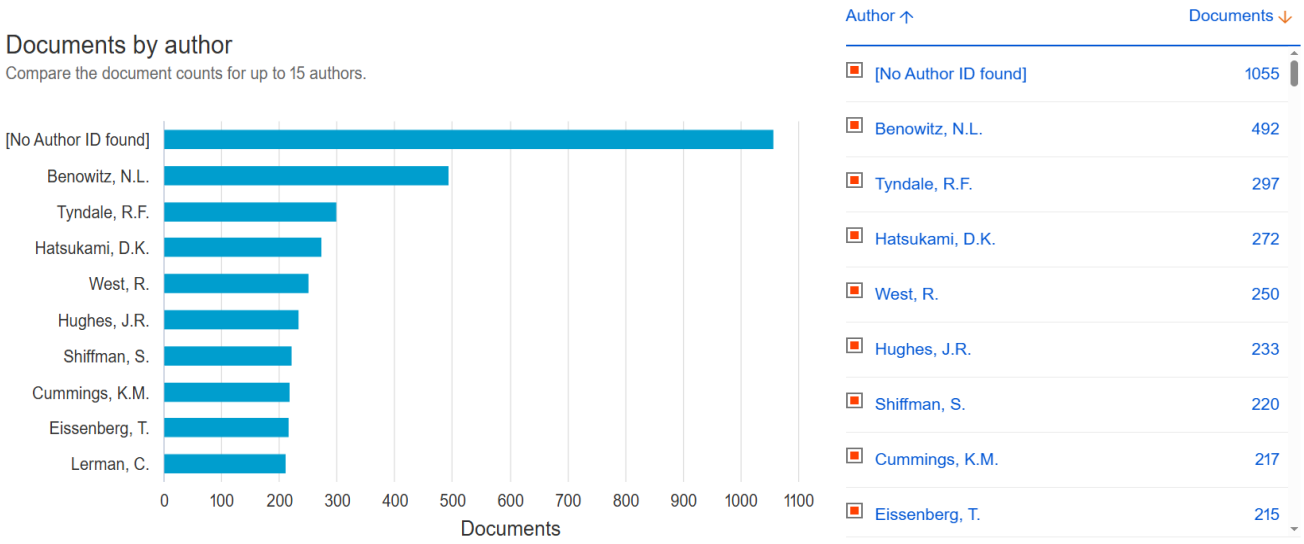

Figure 3: The top ten published authors

This mini review aims to evaluate nicotine not only as an addictive agent, but also as a molecule of biomedical interest, for supervised therapeutic use based on solid experimental data.

2. History of Nicotine

The first seeds of *Nicotiana Tabacum* were introduced to Europe around 1520, following the great transatlantic explorations. Very quickly, the plant was cultivated in Portugal, where it was used for medicinal purposes, in accordance with the humoral theories still dominant in 16th-century European medicine. In 1561, Jean Nicot, the French ambassador in Lisbon—whose name would later be given to the genus *Nicotiana*—sent finely ground tobacco leaves to the French court, intended to relieve the migraines of Queen Catherine de Medici. Seduced by the supposed beneficial effects of the plant, Catherine de Medici authorized its cultivation in Brittany, Gascony, and Alsace. The plant then acquired strong symbolic and social value, and was nicknamed "the Queen's herb." Its use by nasal inhalation (or "presumptive inhalants") first became widespread at the royal court before spreading more widely. However, this popularization of tobacco aroused resistance: certain doctors and theologians of the time saw it as a suspect practice, comparable to witchcraft, because of its unusual physiological effects (P. W. Black et J. Goodman 1995; R. Doll, 1999). By the 17th century, tobacco was firmly established in European cultural habits. Molière attests to this in his comedy Don Juan 1665, writing: "He who lives without tobacco is not worthy of living!" This phrase reflects the growing craze for tobacco at this time, marking the beginning of its global spread: by the end of the 16th century, it was known and used in England, Italy, Germany, but also in Turkey, Morocco, Korea, and many other regions (P. W. Black et J. Goodman 1995; R. Doll, 1999). Jean Nicot's historical importance is such that, several centuries later, in 1809, a French chemist, Louis Nicolas Vauquelin, a professor at the Paris School of Medicine, isolated an active alkaloid present in the plant and named it "nicotine," in homage to the 16th-century diplomat. This discovery marked an important step in the scientific understanding of the physiological properties of tobacco, initiating the plant's transition from a traditional medicinal object to a product studied in the context of modern chemistry (Black et Goodman 1995). **Figure 4** presents the portraits of Jean Nicot, who introduced tobacco to France in the 16th century, and Louis Nicolas Vauquelin, the chemist who identified nicotine in the early 19th century (Dorveaux, 1932; Haas, 1992).

Table 1 traces the main stages in the history of nicotine, from the discovery of the *petum* plant in America and the introduction of tobacco in Europe in the 16th century to the chemical identification of the alkaloid in the 19th century. It highlights the major contributions of figures such as Jean Nicot and Louis Nicolas Vauquelin.

Figure 4 : Portraits of Jean Nicot and Louis Nicolas Vauquelin.

Table 1: Historical landmarks related to nicotine

Dates	Events	References
1492	Christopher Columbus discovered America and noticed that the Indians smoked a plant called "*petum*".	(Stolberg, 2008)
1520	The first tobacco seeds are brought back to Europe.	(Russo *et al.* 2011)
1561	Jean Nicot sends tobacco leaves to Catherine de Medici.	(Gilman et Zhou, 2004)
1809	Nicotine was discovered by Louis Nicolas Vauquelin.	(Russo *et al.* 2011)
1830	The first industrially produced cigarettes appear.	(Russo *et al.* 2011)
1943	The first cigarette-making machine is invented.	(Russo *et al.* 2011)
1950-today	The first epidemiological studies prove the toxicity of tobacco.	(Russo *et al.* 2011)

3. Plant Origin of Nicotine

Solanaceae, commonly called "nightshades" or referred to as "plants of the *Solanaceae* family," are a large family of flowering plants belonging to the order *Solanales*. Shown in **Figure 5**, this family includes approximately 2,700 species distributed throughout the world. Native mainly to South and Central America, Solanaceae are now present on all continents, demonstrating their strong capacity for adaptation and dispersal (M. R. Lee, 2006; P. . Houghton, 2004; S. Knapp, 2002).

Several species in this family are of significant economic, nutritional, or medicinal importance. Some have high alkaloid concentrations, making them highly toxic. In contrast, others, such as the tomato (Solanum lycopersicum), the potato (Solanum tuberosum), the eggplant (Solanum melongena), and the chili peppers (Capsicum), are commonly consumed as food. Some of these species are shown in **Figure 6** (S. Knapp, 2002; R. G. Olmstead et L. Bohs 2007).

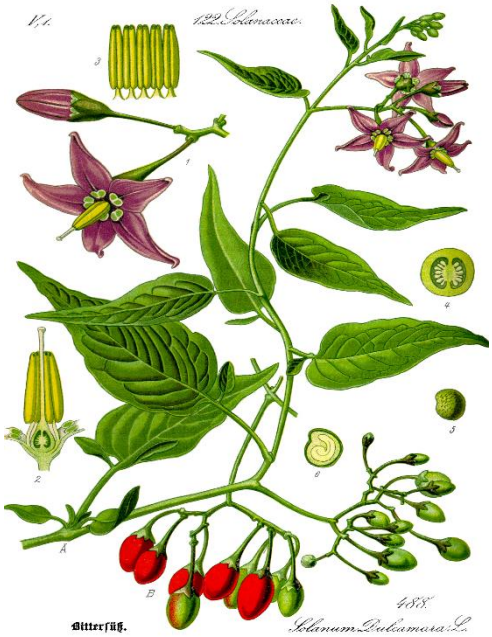

Figure 5 : Family Solanaceae: Solanum dulcamara.

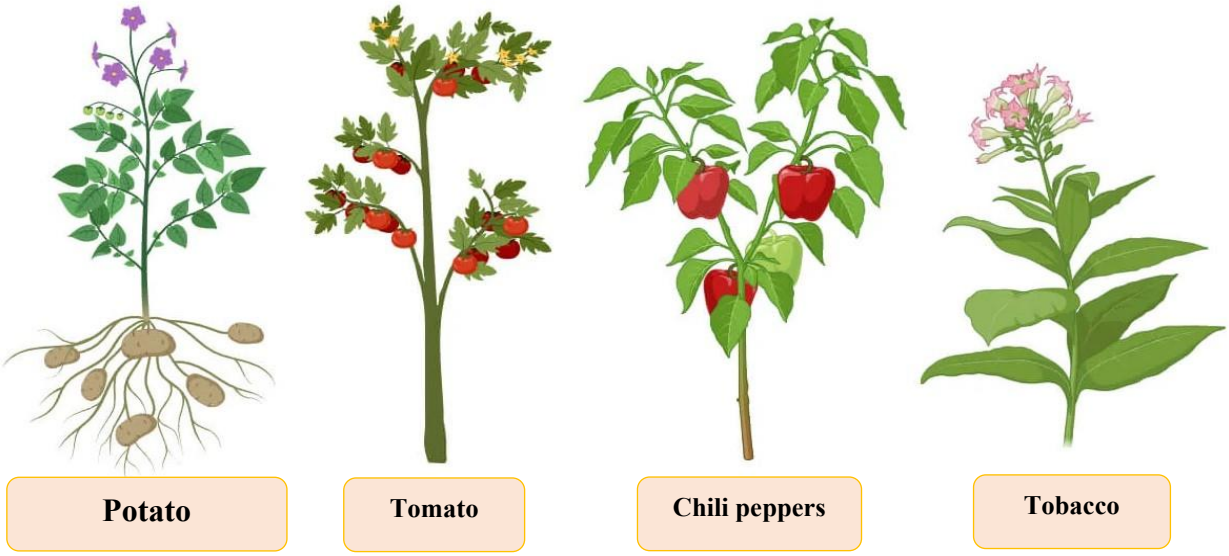

Figure 6 : Some species of the Solanaceae family: potato, tomato, chili pepper and tobacco.

Species such as *deadly nightshade – Atropa belladonna – black nightshade – Solanum nigrum – datura – Datura stamonium –* and *tobacco – Nicotiana tabacum –* are known for their medicinal, psychotropic, and toxic properties. The traditional and modern uses of these plants vary according to cultural and scientific contexts, ranging from herbal medicine to recreational and ritual uses. Tobacco, in particular, has been used for centuries as a psychoactive substance due to its high content of nicotine, a powerful alkaloid with neurostimulator effects (P. . Houghton 2004; S. Knapp, 2002; R. G. Olmstead et L. Bohs 2007). The concentration of active compounds gives certain Solanaceae a unique place at the interface

between food, medicine, ethnobotany, and toxicology. Among the many Solanaceae, *Nicotiana tabacum* stands out for its high nicotine content and its very specific uses. It will be the subject of the following section.

4. Nicotiana Tabacum

Tobacco – Nicotiana tabacum – is an annual herbaceous plant of the Solanaceae family, primarily cultivated for its leaves, which are rich in nicotine (alkaloid). Used in the manufacture of manufactured tobacco, this plant is sometimes referred to as "tall tobacco" or "Nicot grass". The generic name Nicotiana recalls the historical contribution of Nicot, while the specific epithet tabacum derives from a word of Arawak origin – Tobacco – which originally designated the rolls of leaves smoked by the indigenous populations of the Antilles, notably in Haiti and Cuba, during the encounter with Christopher Columbus in 1492.

Figure 7 : Image illustrating the Nicotiana tabacum plant.

Nicotiana tabacum is characterized by rapid growth and a robust morphology. It can reach a height of 1 to 3 meters. Its thick, erect, circular stem has few branches. Branching is generally more pronounced in the upper part of the plant. The taproot system is long and fibrous (N. Ren et M. P. Timko, 2001; D. Garon et J.-C. Guéguen 2020). The leaves, numerous, entire, and large (30 to 60 cm), are sessile, alternate, and slightly decurrent. Their shape varies from oval to lanceolate, with a pointed tip. Their texture is fragile and sticky due to the presence of secretory hairs. They emit a sweet odor intended to attract pollinators, but also contain repellent substances such as nicotine. The flowering consists of terminal inflorescences formed of tubular flowers, the color of which varies depending on the variety: yellowish-green, white, or pinkish (N. Ren et M. P. Timko, 2001; D. Garon et J.-C. Guéguen 2020).

6. Chemical Structure of Nicotine

Nicotine ($C_{10}H_{14}N_2$) is the main addictive agent associated with tobacco consumption. It is a heterobicyclic, pyridine-pyrrolidic alkaloid, and represents about 5% of the dry mass of the tobacco leaf and 90-95% of the total alkaloids it contains. Although concentrated mainly in Nicotiana tabacum and some related species, very low traces are also detectable in other Solanaceae, such as tomato, potato and eggplant (W. Zhang *et al.*, 2024; E. F. Domino, E. Hornbach, et T. Demana 1993). Structurally (**Figure 7**), nicotine is a bicyclic compound combining a pyridine ring with a pyrrolidine ring. The systematic nomenclature of UPAC and NIH designates them as 3-(1-methyl-2-pyrrolidinyl)pyridine. Its structural formula [1-methyl-2-(3-pyridyl)pyrrolidine] was deduced in 1892 and finally confirmed by total synthesis three years later (D. Yildiz, 2004).

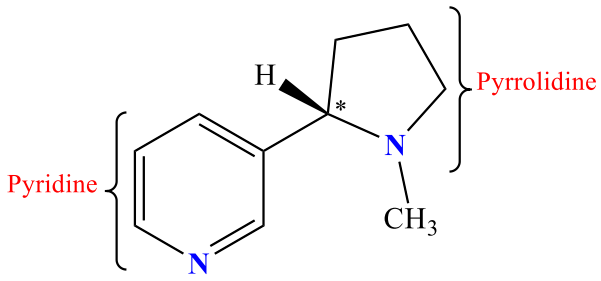

Figure 8 : Chemical structure of nicotine.

The molecule has a single stereogenic center on carbon 2 of the pyrrolidine ring, giving rise to two enantiomers. In nature, nicotine only exists in the (S) form, which is levorotatory. The (R) enantiomer only appears during chemical syntheses or thermal racemizations. These two enantiomers are shown in **Figure 9** (N. Le Novere et J. P. Changeux, 1995; P. M. Clayton, 2013; P. A. Crooks 1999).

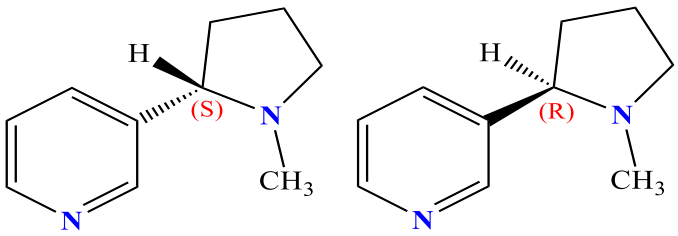

Figure 9 : Chemical structure of (S)-nicotine and (R)-nicotine.

Precise knowledge of the structure of nicotine is essential for understanding its physicochemical properties, which are discussed in the next section.

7. Physicochemical properties:

The alkaloids present in tobacco, of which nicotine is the main representative, are classified among the weak organic bases. Nicotine, in particular, has two tertiary amine groups that give its molecule a notable basic character. In its pure state, it appears as a clear, slightly oily liquid with a pungent pyridine odor.

However, this free form is chemically unstable; when exposed to air and light, it undergoes progressive oxidation, resulting in a color change from pale yellow to dark brown. This oxidation, linked to heat, makes it more viscous (D. Yildiz 2004; P. A. Crooks 1999). This degradation process, accelerated by heat, is likely linked to oxidation reactions involving free radicals. Nicotine solutions subjected to these conditions undergo rapid chemical aging, demonstrating the molecule's sensitivity to oxidizing agents (P. A. Crooks 1999). Furthermore, nicotine is a very hygroscopic substance. It readily forms soluble salts upon contact with many acids and certain metal ions. It also exhibits a strong affinity for organic solvents, allowing for easy extraction from aqueous solutions. Its boiling point is 247 °C (P. A. Crooks 1999). Finally, nicotine can react violently with strong oxidizing agents, which justifies strict precautions when handling it in a chemical or industrial context ((D. Yildiz 2004). Nicotine is a central compound in the study of tobacco, both for its historical role and its chemical implications. Discovered by Vauquelin in the leaves of Nicotiana tabacum, it owes its name to Jean Nicot, an emblematic figure in the introduction of tobacco to France. Its complex structure and unique physicochemical properties—instability to light, optical rotation, and solubility in organic solvents—make it a molecule of great scientific, pharmacological, and industrial interest. Having explored its origin, structure, and fundamental characteristics, it is now essential to study the processes for obtaining this molecule from plant material or through synthesis.

8. Synthesis and extraction methods

Having studied the fundamental characteristics of nicotine, it is now appropriate to examine the different methods for obtaining it, either by extraction from the Nicotiana tabacum plant or by chemical synthesis in the laboratory. These approaches have varying benefits depending on the objectives: industrial production, scientific research, or the development of alternative products (such as nicotine substitutes). In this chapter, we will first discuss the main routes for the chemical synthesis of nicotine, then examine some of its derivatives, before presenting the extraction processes from the Nicotiana tabacum plant.

9. Nicotine Synthesis Methods:

9.1. Synthesis of (S)-nicotine:

Due to the relative simplicity of the (S)-nicotine molecule, its commercial availability, and its low cost, examples of enantioselective synthesis are relatively rare. Furthermore, (S)-nicotine can be easily racemized, and the two enantiomers, (R)- and (S)-nicotine, are easily separable. Nevertheless, a method for the enantioselective synthesis of (S)-nicotine has been described by Chavdarian et al (Chavdarian et al., 1982), using the amino acid L-proline as a precursor. This route is shown in **Figure 10** (Crooks 1999; Chavdarian et al., 1982).

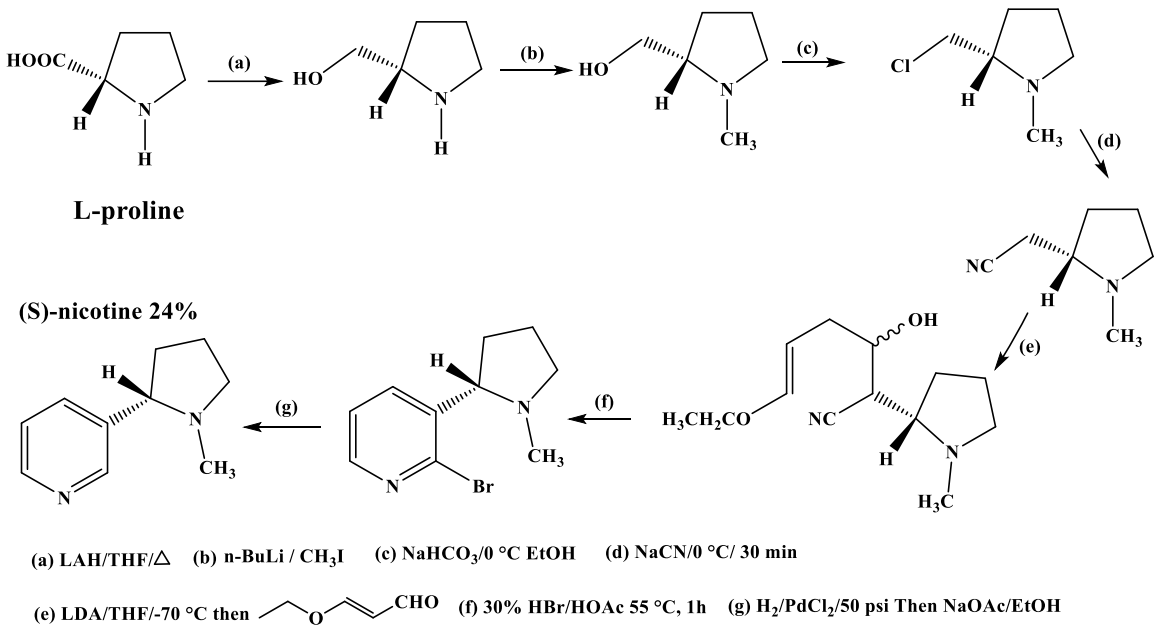

Figure 10: Synthesis of (S)-nicotine from L-proline

Thus, another method for the synthesis of (S)-nicotine was developed from 3-bromopyridine as the starting compound. The corresponding reaction scheme is shown in **Figure 11** (Wagner et D. L. Comins, 2007; J. Pandey, 2021). **(a)** The formation of hydroxyketone begins with a halogen-lithium exchange reaction between 3-bromopyridine and n-BuLi, generating a lithium intermediate. This is then trapped by lactone, leading to hydroxyketone. (**b)** The oxidation of OH from hydroxyketone to the aldehyde (pyridin-3-yl)-4-oxobutanone is achieved via the Swern oxidation, a mild method that uses oxalyl chloride ($COCl_2$), dimethyl sulfoxide (DMSO), and a triethylamine base (NEt_3). This reaction selectively produces the aldehyde without strong oxidizing conditions, avoiding the degradation of sensitive substrates. (**c)** The compound results from the condensation of the aldehyde with the galactosylated amine α,2,3,4,6-tetra-O-pivalolyl-β-D-galactopyranosylamine, leading to the formation of an amine. (**d)** The final step consists of acid hydrolysis carried out in a mixture of MeOH and 1M HCl, allowing the release of (S)-nornicotine, a precursor which, after alkylation, leads to (S)-nicotine.

9.2. Synthesis of (R)-nicotine:

A method for the synthesis of (R)-nicotine was developed using pyridinecarboxaldehyde as the starting substrate, reacting with β-allyldiisopinocampheylborane as a chiral reagent. This approach allows for the controlled introduction of chirality during allylation. The reaction scheme detailing this synthesis is shown in **Figure 12** (Pandey et al., 2021).

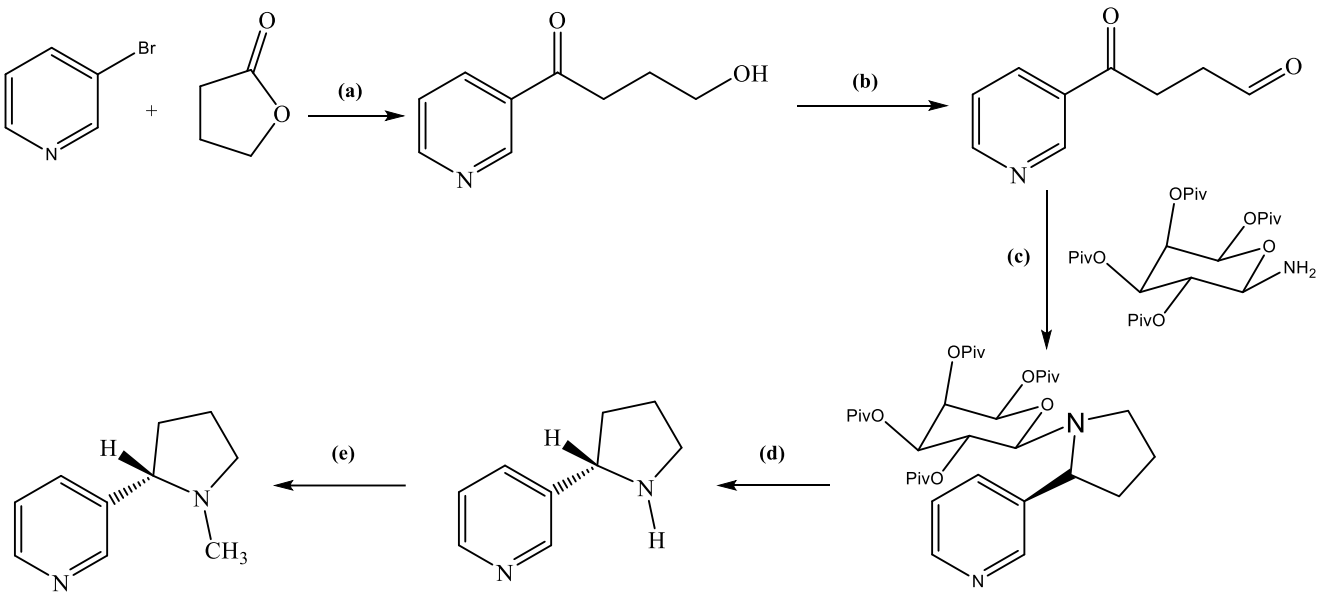

Figure 11: Synthesis of (S)-nicotine (92%) from bromopyridine

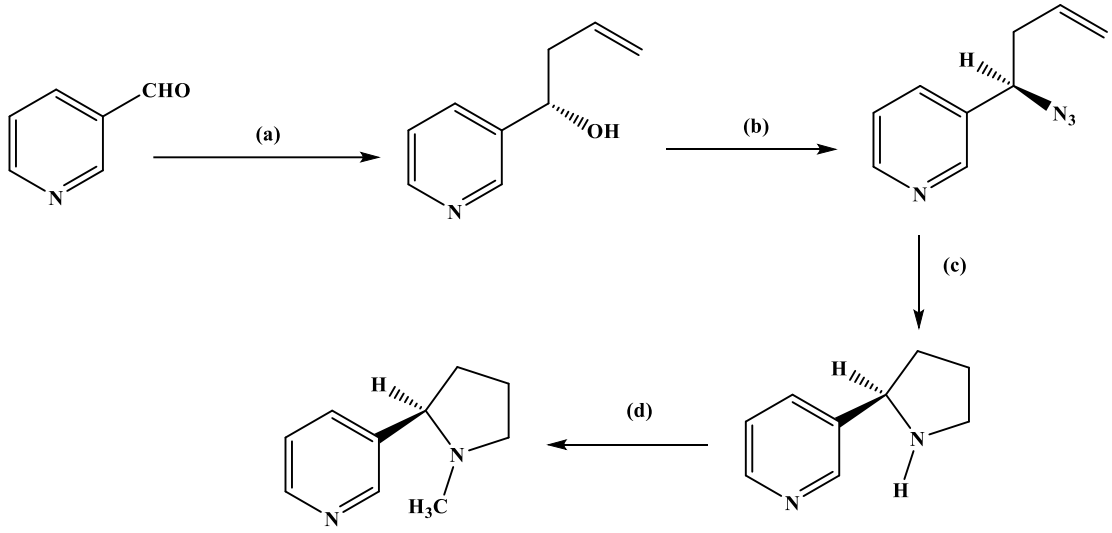

Figure 12: Synthesis of (R)-nicotine via pyridine carbaldehyde with 92%

(a) Enantioselective allylation:The synthesis begins with an asymmetric allylation of pyridinecarboxaldehyde using β-allyldiisopinocampheylborane in diethyl ether at 100 °C. This reaction produces (S)-homoallyl alcohol in 86% yield.

(b) **(b)** Formation of the chiral azide via the Thompson reaction: The alcohol is then converted to a chiral azide by a Thompson reaction, using DBU as the base and diphenylphosphorylazide in toluene. This transformation occurs in 90% yield and without loss of chirality. The Thompson reaction is a gentle method for converting an activated alcohol to an azide, via a mechanism involving hydroxyl group activation and internal nucleophilic substitution, preserving the stereochemical configuration.

(c) (**c)** Intramolecular Hydroboration and Cyclization: The azide compound then undergoes intramolecular hydroboration, catalyzed by disiamylborane [$B(C_6H_{11})H$] in THF. Boron preferentially binds to the less substituted carbon of the double bond. The formation of a nitrogen-boron complex induces cyclization, via the migration of an alkyl group from boron to nitrogen with expulsion of dinitrogen (N_2), leading to the closure of the pyrrolidine ring.

(d) (**d)** Final Alkylation to (R)-nicotine: The (R)-nornicotine obtained is then alkylated to generate the final product, (R)-nicotine, according to a two-step protocol: - Activation of the amine function by reaction with EtOCOCl in the presence of Et3N in diethyl ether. - Reduction of the carbamate intermediate using $LiAlH_4$ in THF at 0 °C, allowing to restore amine III and form (R)-nicotine.

10. Nicotine Derivatives:

After exploring the main asymmetric synthesis pathways for obtaining the two enantiomers of nicotine, it is relevant to examine the structural diversity that this molecule allows. Indeed, nicotine constitutes an interesting chemical platform for the design of derivative compounds, whether of pharmacological, agrochemical, or other interest. This section focuses on presenting some nicotine derivatives, **Figure 13,** (Pogocki et al., 2007; Smith et al. 2006).

In addition to chemical synthesis approaches and the study of some nicotine derivatives, it is also appropriate to examine the processes allowing its direct extraction from plant material. The following section is devoted to the main methods of nicotine extraction from *Nicotiana tabacum*.

11. Nicotine Extraction Methods:

Several methods for extracting nicotine from tobacco are well documented and can be performed in a standard laboratory. These methods include liquid-liquid extraction using concentrated aqueous sodium hydroxide (NaOH) solution, followed by extraction of nicotine with an organic solvent such as dichloromethane (Cl_2CH_2). This method is based on the conversion of nicotine into its free, more lipophilic basic form, facilitating its transfer into the organic phase. However, dichloromethane also solubilizes many other substances present in the plant material, including colored compounds, minor alkaloids, and organic impurities, which limits the purity of the resulting product.

A more selective alternative is steaming distillation (SDE), described in several experimental studies. This method relies on the relatively high volatility of nicotine and produces an extract with a purity of up to 95%, in the form of a yellowish oil. In addition to its simplicity, this technique has the advantage of reducing the use of toxic organic solvents. It should be noted, however, that handling nicotine,

particularly in its concentrated or pure form, requires strict precautions due to its high toxicity. All operations must be conducted under a properly functioning fume hood, while wearing gloves, goggles, and a lab coat. Increased vigilance is required, in particular to avoid accidental inhalation of its vapors or any direct contact with the pure product (Yildiz , 2004; Reichl, 2010). Generaly by introducing approximately 150 mL of distilled water into a 250 mL steam generator flask. In a second flask, intended for distillation, place 5 g of finely ground tobacco and 50 mL of a 30% aqueous sodium hydroxide (NaOH) solution.

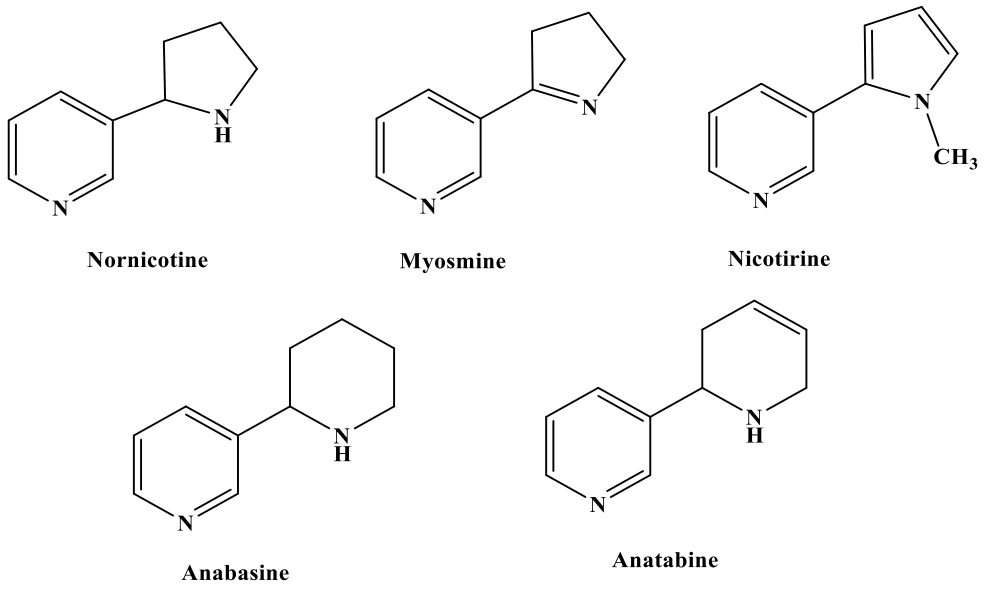

Figure 13: Some nicotine derivatives.

After assembling the steam distillation setup, bring the generator flask to a boil to ensure a constant flow of steam into the distillation flask. Distillation is continued until approximately 75 mL of distillate is collected. Unlike some steam distillations involving hydrophobic compounds, nicotine here exhibits good solubility in water, resulting in a single, homogeneous aqueous phase. The yellowish distillate is transferred to a separating funnel. Nicotine extraction is then performed using three successive washes with 20 mL of dichloromethane. The organic phase, which takes on a yellow color, separates clearly from the aqueous phase which has become colorless, indicating efficient extraction of nicotine into the organic solvent. The organic fractions are combined and then dried over anhydrous sodium sulfate. After filtration, the solvent is removed by evaporation under reduced pressure using a rotary evaporator. Approximately 100 mg of a yellow oily residue is finally obtained. After steam distillation of nicotine, it is essential to confirm the identity and assess the purity of the resulting compound. Since nicotine is an alkaloid with well-defined physicochemical properties, several analytical techniques can be used to ensure the characterization and identification of this extracted product. Commonly used methods include 1H NMR spectroscopy, 13C NMR spectroscopy, UV-visible spectroscopy, Fourier transform infrared

spectroscopy FTIR, and high-performance liquid chromatography HPLC. These complementary approaches ensure rigorous and reliable characterization of the extracted product (Clayton et al. 2013; R. S. Dawood et R. A. Stockman, 2025). Nicotine, the main alkaloid in tobacco, can be obtained either by chemical synthesis or by extraction from the plant. Synthetic methods, although rarely implemented due to the molecule's natural availability, enable the production of the (S)- and (R)-nicotine enantiomers, with variable yields and enantioselectivity depending on the approach used. In parallel, more accessible extraction processes, such as steam distillation, allow for the efficient isolation of nicotine from tobacco in the laboratory. These different production routes must be complemented by rigorous identification and characterization methods to confirm the chemical nature of the extracted or synthesized product and assess its purity. Thus, the combined study of synthesis, extraction, and characterization methods allows for an understanding of nicotine in all its complexity.

12. Addictive effects and therapeutic potentials of nicotine

Nicotine is widely recognized for its central role in the development of tobacco addiction, primarily due to its powerful effects on brain reward circuits. However, beyond its addictive profile, this molecule is of growing interest in the pharmacological and biomedical fields due to its neuromodulatory, cognitive, and anti-inflammatory properties. This chapter explores this duality: on the one hand, the biological mechanisms underlying nicotine addiction, and on the other, the promising therapeutic applications this molecule offers. Nicotine is a pyrrolidine alkaloid naturally present in tobacco and is one of the leading agents responsible for tobacco addiction. Its high addictive power results from its interaction with the brain's reward system, particularly through the stimulation of nicotinic acetylcholine receptors (nAChRs), α4β2, located in dopaminergic neurons of the mesolimbic pathway (**Figure 14**). This activation induces a massive release of dopamine, causing feelings of pleasure, well-being and positive reinforcement of consumption (J. A. Dani et S. Heinemann, 1996; Machold *et al.* 1995).

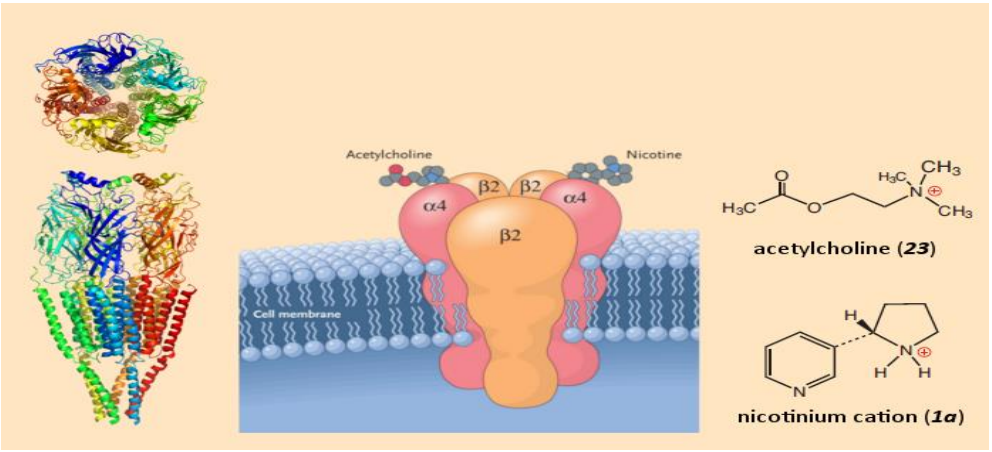

Figure 14: Nicotinic acetylcholine receptors.

Chronic nicotine exposure leads to desensitization of nAChRs, which contributes to the development of tolerance and withdrawal symptoms upon cessation of use, including irritability, anxiety, agitation, impaired concentration, and craving (De Biasi et Dani, 2011). Toxicologically, nicotine is a potentially lethal substance at high doses. The lethal dose has been estimated at 30–60 mg, although recent studies suggest a higher range, between 500 and 1000 mg, due to tolerance developed in regular users. However, accidental ingestion of relatively small amounts can be fatal, particularly in children (Mayer, 2014). From a public health perspective, tobacco use—the main source of nicotine exposure—is one of the leading preventable causes of death worldwide. According to the World Health Organization (WHO), it is responsible for more than 8 million deaths each year. These deaths are mainly due to cardiovascular diseases, cancers (particularly lung cancer) and chronic respiratory pathologies caused or aggravated by tobacco.

13. Therapeutic Potential of Nicotine:

Despite its well-documented addictive properties, nicotine has significant therapeutic potential in various medical settings, primarily due to its specific interaction with nicotinic acetylcholine receptors (nAChRs). These receptors play a key role in modulating the release of several neurotransmitters (dopamine, glutamine, GABA) as well as in regulating the body's inflammatory responses. In the field of neurodegenerative diseases, nicotine has demonstrated significant neuroprotective effects. In Alzheimer's disease, for example, it appears to improve specific cognitive functions by stimulating the activity of nAChRs (Cao *et al.,* 2024). In psychiatric disorders, particularly schizophrenia, nicotine improves attention and corrects certain deficits in intrinsic brain activity, particularly through the activation of nicotinic receptors. This could explain the high prevalence of smoking among schizophrenic patients, who use nicotine as a form of self-medication to compensate for cognitive dysfunction (Cao *et al.,* 2024). Its anti-inflammatory action, via the anti-inflammatory cholinergic pathway (nAChR α7), is also being studied to treat certain autoimmune and chronic inflammatory diseases such as ulcerative colitis or rheumatoid arthritis (Cao *et al.,* 2024). In cancer, the effects of nicotine are complex and ambivalent. Although not considered a direct carcinogen, nicotine may modulate certain mechanisms involved in tumor progression, particularly through the activation of nAChR receptors on cancer cells. Recent research explores the possibility of nicotine derivatives for antitumor purposes (Wang et Hu 2014). Nicotine embodies a marked pharmacological duality. While recognized for its high addictive potential, it nonetheless remains a promising therapeutic candidate in several medical fields. This ambivalence stems from its interaction with nicotinic acetylcholine receptors, which are involved in both dopaminergic reward mechanisms, the origin of addiction, and the modulation of neurocognitive, immune, and anti-inflammatory functions. Current data suggest potential

benefits in neurology, psychiatry, and immunology, but also highlight the need for careful assessment of the risks associated with nicotine use, particularly in terms of tolerance and withdrawal. A detailed understanding of this molecule could pave the way for new targeted therapeutic approaches that account for its inherent adverse effects. Biomolecules extracted from natural sources offer a wide array of applications, but their potential toxicity must be carefully assessed (Mungwari *et al.,* 2025; Cherriet *et al.,* 2023; Haddou *et al.,* 2023; Diass *et al.,* 2023; Schoental, 1965). While many biomolecules exhibit beneficial properties, such as biodegradability, biocompatibility, and bioactivity, some can also be toxic or have adverse effects. Careful consideration of the source of the plants and extraction methods may identify potential risks associated with these biomolecules, which is crucial for the safe and effective use of these biomolecules in various fields, such as pharmaceuticals, food, and cosmetics.

Conclusion

Nicotine, the principal alkaloid of tobacco, is a multifaceted subject of study, spanning botanical, chemical, pharmacological, and medical disciplines. Exploring its history and botanical origins has helped situate this molecule within a rich cultural and scientific context, marked by the long-standing use of tobacco and a gradual evolution in our understanding of its effects. Chemically, nicotine has a complex heterocyclic structure, consisting of two enantiomers: (R)-nicotine and (S)-nicotine, whose pharmacological properties differ markedly. This stereochemical distinction is essential in chemical synthesis, extraction, and characterization approaches. The study of these methods, particularly steam distillation, has illustrated the feasibility of obtaining pure nicotine under laboratory conditions while highlighting the rigorous precautions required due to its toxicity. Analytical characterization techniques, such as NMR, UV, FTIR, and HPLC, enable us to confirm the identity and purity of the isolated compound. Finally, nicotine reveals a fascinating pharmacological duality: on the one hand, it is a highly addictive substance, acting on the dopaminergic reward system; on the other, it demonstrates growing therapeutic potential in diverse areas such as neurodegenerative diseases, psychiatric disorders, inflammatory pathologies, and even certain cancers. This ambivalence poses a major ethical and scientific challenge: how to exploit the beneficial properties of nicotine while minimizing its dangerous effects?

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