Journal of Current Pharma Research (JCPR)

Volume 21, Issue 7, July 2025 **jcpr.humanjournals.com** ISSN: 2230-7842, 2230-7834

Chemical Nomenclature of Antihistamines and Neuroleptics with Phenothiazine Core According to the International Union of Pure and Applied Chemistry

Soufiane El Marrakchi*[1], Jihane Ifezouane[1], Baderddine. Moukafih[1], Ismail Bennani[1], Jaouad El Harti[2], Jamal Lamsaouri[2], Abdeslam El Kartouti[1]

1 Sidi Mohamed Ben Abdellah University, Faculty of Medicine, Pharmacy and Dental Medicine, Department of Pharmaceutical Sciences, 31000 Fez, Morocco.
2 Mohammed V University, Faculty of Medicine and Pharmacy,Therapeutic Chemistry Laboratory, 6203 Rabat, Morocco.

Received: 2025-06-20 Revised: 2025-07-10 Accepted: 2025-07-25

ABSTRACT :

Phenothiazines are well-known organic compounds in the field of organic chemistry. Initially used as dyes, they have been employed as pharmaceutical agents for a very long time. Today, they are found in molecules exhibiting neuroleptic, antihistaminic, and other pharmacological properties. From a chemical standpoint, they consist of three ortho-fused rings in their structure. Their chemical nomenclature is complex and multifaceted, but the standardized nomenclature of The International Union of Pure and Applied Chemistry is preferred, although other types of nomenclature exist. This work highlights the chemical nomenclature of phenothiazine cores used in two pharmacological classes: antihistamines and neuroleptics.

Keywords: Antihistaminic, Neuroleptic, IUPAC nomenclature, Phenothiazine

INTRODUCTION

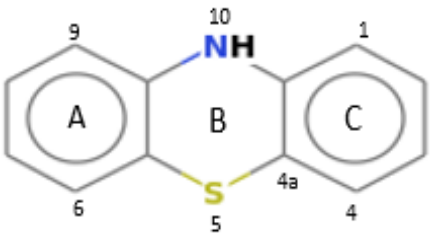
The phenothiazine core is widely used in medicinal chemistry due to its significant pharmacological potential [1]. This chromophore is found in active ingredients treating allergies specifically, phenothiazine-core antihistamines [2] which represent one of the most utilized drug classes for managing various allergic conditions [3]. This core structure is also utilized for the synthesis of various active pharmaceutical ingredients with neuroleptic properties [4].

This work highlights the chemical nomenclature of selected phenothiazine-core antihistamines and neuroleptics. The nomenclature follows the standards of the International Union of Pure and Applied Chemistry (IUPAC) [5].

International Union of Pure and Applied Chemistry (IUPAC) [6]

The International Union of Pure and Applied Chemistry is an international organization established over a century ago (in 1919). IUPAC operates under the governance of multiple chemical societies and academies of sciences, supplemented by voluntary individual members. Its core activities involve standardizing the nomenclature system for organic compounds and maintaining updates to the periodic table of chemical elements. IUPAC's scientific activities are overseen by eight divisions. Division VIII, chaired by Dr. Michelle Rogers, leads the project « Corrections, Revisions, and Extensions for the Nomenclature of Organic Chemistry - IUPAC Recommendations and Preferred Names 2013 (the IUPAC Blue Book) » [5].

Nomenclature of the Phenothiazine Core



The phenothiazine core constitutes a dibenzothiazine system, comprising three rings designated A, B, and C. This structure belongs to the class of ortho-condensed polycyclic heterocycles, where ring B is a thiazine heterocycle.

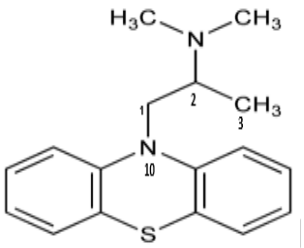
Journal of Current Pharma Research (JCPR)
Volume 21, Issue 7, July 2025 jcpr.humanjournals.com ISSN: 2230-7842, 2230-7834

The system numbering begins from the rightmost ring (ring A or C), assigning the lowest locant to one of its vertices. The numbering direction follows the path that gives the sulfur heteroatom the lowest possible locant, while respecting the priority order O > S > N. The numbering then continues throughout the cyclic framework. Carbon atoms shared between two adjacent rings are designated by preceding letters of the alphabet.

Ring B exhibits saturation patterns, commonly referred to as hydrogenation. The thiazine ring features only one saturation site between the heteroatom and an adjacent carbon, identified by a hydrogen at vertex number 10. This is referred to as an indicated hydrogen, denoted in nomenclature by a capital H. The core system is thus named *10H-phenothiazine*.

Nomenclature of Selected Phenothiazine Antihistamines

Either the International Nonproprietary Name : Promethazine



Principal Functional Group : Amine, specifically, a tertiary amine.

Parent chain : Propane, which is the longest carbon chain bearing the main functional group and the substituents. The numbering direction of the parent chain is determined first by the position of the amine functions, followed by that of the substituents, which must have the lowest locants.

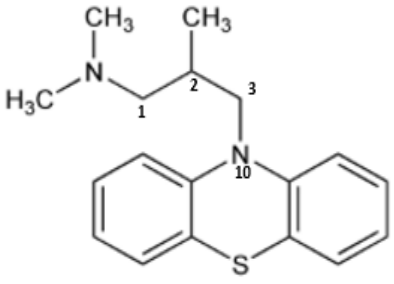
The amine function is attached at position 2 on propane. The propane chain can be numbered in either direction, with priority given first to the principal functional group (which must receive the lowest locant), then to substituents: propan-2-amine. (The (e) of 'propane' is dropped when two vowels would otherwise appear consecutively.)

Substituents (listed in alphabetical order): *N,N*-dimethyl-1-phenothiazin-10-yl. The alphabetical order considered is based on (m) for methyl and (p) for phenothiazine. The *N,N* and (-di) prefixes designating the two methyl substituents on the amine function are not considered in the alphabetical ordering.

The phenothiazine is attached via position 10 to position 1 of the parent chain : phenothiazin-10-yl (yl indicating an alkyl group). In our case, this is 1-phenothiazine. (The (e) of phenothiazine is dropped when preceding the vowel (y).)

Chemical Name : *N,N*-dimethyl-1-(phenothiazin-10-yl)propan-2-amine. Substituents are positioned before the parent chain name, while the principal functional group is always suffix.

-Either the International Nonproprietary Name : Alimemazin



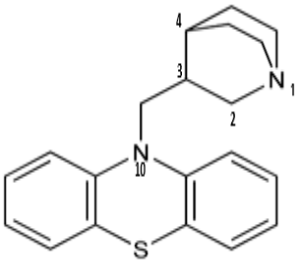
Principal Functional Group : Amine.

Parent chain : Propane. The amine function must be assigned the lowest locant when attached to propane: propan-1-amine or propanamine.

Substituents : There are three methyl groups, two of which are attached to the principal functional group. The phenothiazine is incorporated into the parent chain at carbon 3. Ils sont classés suivant l'ordre alphabétique de la première lettre du méthyle, suivi de la phénothiazine.

Chemical Name : *N,N,2*-trimethyl-3-(phenothiazin-10-yl)propan-1-amine.

-Either the International Nonproprietary Name : Mequitazine



Principal Functional Group : Unidentified. The phenothiazine system (alkyl phenothiazine) will be taken into consideration.

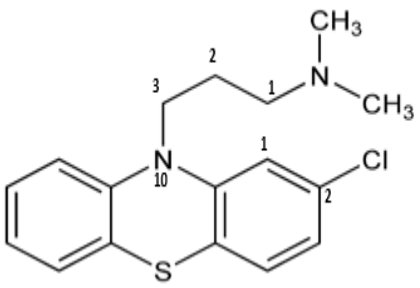
Parent chain : Phénothiazine.

Substituents : The bicyclic framework represents a bridged polycyclic heterocyclic systemThe parent hydrocarbon name derives from the eight-atom open-chain equivalent : octane. The name is prefixed by 'bicyclo-' to denote the two fused ring systems. The system is numbered starting from a bridgehead atom, which is the heteroatom (nitrogen) assigned the lowest locant (1-aza), and is positioned before the 'bicyclo' name (1-azabicyclo). Numbering continues along the longest branch to the other bridgehead atom, then along the shorter branch back to the starting atom (nitrogen). The number of atoms in the long branch is 2, in the short branch 2, and in the bridge 2, separated by periods and enclosed in square brackets. The system is thus 1-azabicyclo[2.2.2]octane, which corresponds to the quinuclidine ring. The latter is attached to the parent chain at position 3, as the insertion locant must be the lowest possible, which determines the numbering direction of this ring. The structure is 1-azabicyclo[2.2.2]octan-3-yl, functioning as a substituent bound to a methyl group that is itself attached to position 10 of the phenothiazine system.

Chemical Name : 10-(1-azabicyclo[2.2.2]octan-3-ylmethyl)phenothiazine.

Nomenclature of Some Phenothiazine Neuroleptics

-Either the International Nonproprietary Name : Chlorpromazine



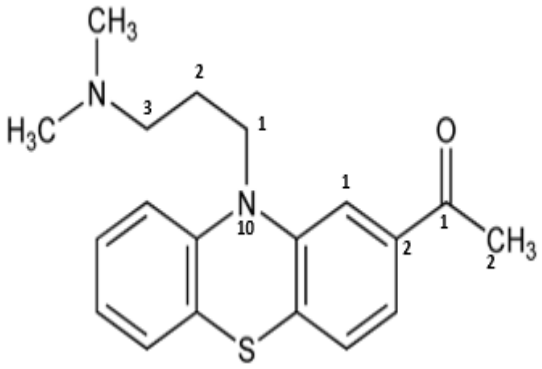
Principal Functional Group : Amine, specifically, a tertiary amine.

Parent chain : Propane, This is the longest carbon chain; the numbering direction is chosen to assign the lowest locant (1) to the amine function : propane-1-amine or propanamine.

Substituents : 2-chlorophenothiazine followed by *N,N*-dimethyl, ordered alphabetically based on the first letter of 'chloro' preceding 'methyl'. The phenothiazine is incorporated into the parent chain via position 10, attached to propane at position 3. The substituent becomes 3-(2-chlorophenothiazin-10-yl).

Chemical Name : 3-(2-chlorophenothiazin-10-yl)-*N,N*-dimethylpropan-1-amine.

-Either the International Nonproprietary Name : Acepromazine



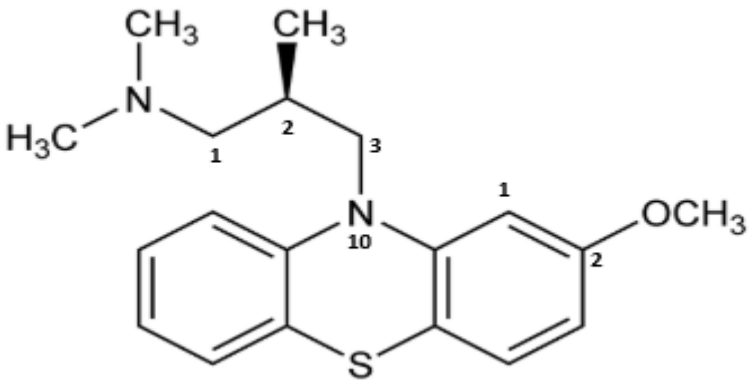
Principal Functional Group : The derivative contains two principal functional groups, amine and ketone. The ketone function takes priority and is placed on the parent chain.

Parent chain : ethane, to which the principal functional group is attached. It is ethan-1-one or ethanone.

Substituents : This is the substituted phenothiazine. The phenothiazine is attached to ethanone at position 1 via its position 2. At position 10, a propylamine chain is inserted; specifically, it is 3-(dimethylamino)propyl. The substituent name becomes 10-[3-(dimethylamino)propyl]phenothiazin-2-yl, ordered alphabetically according to the first letter of 'methyl', followed by 'phenothiazine'.

Chemical Name : 1-[10-[3-(dimethylamino)propyl]phenothiazin-2-yl]ethanone.

-Either the International Nonproprietary Name : Levomepromazine



Principal Functional Group : Amine. The ether function is not considered in IUPAC chemical nomenclature.

Parent chain : Propane, with the amine function attached to the lowest position, which is 1. This gives either propane-1-amine or propanamine.

Substituents : 2-methoxyphenothiazine. The ether group is attached at position 2 on the phenothiazine ring, which itself is attached at position 3 to the main chain from its 10-position. This gives 3-(2-methoxyphenothiazin-10-yl). The second substituent is the dimethyl group, attached to the main amine function, and the methyl group, attached at position 2 of the propane. The alphabetical order taken into consideration is that of (o) for methoxy and (y) for methyl. The *N,N* and (-tri) prefixes referring to the three methyl substituents on the amine function are not considered in the alphabetical ordering.

Chemical Name : 3-(2-methoxyphenothiazin-10-yl)-*N,N*,2-trimethylpropan-1-amine.

Conclusion

Although the nomenclature of organic chemical compounds employs several synonyms, IUPAC nomenclature remains the gold standard in this field. While it requires the expertise of chemists and academicians, it nevertheless remains complex. Our work has highlighted the nomenclature of the phenothiazine ring, a chromophore with significant therapeutic potential, given its widespread use in the synthesis of antihistamine and neuroleptic drugs. It highlights another scientific aspect of pharmaceutical chemistry that is not commonly used in pharmaceutical terminology. Chemical nomenclature remains a harmonized means of communication among chemists, pharmacists, and clinicians within and across countries. Its significance extends beyond these considerations: IUPAC-standardized chemical nomenclature is routinely referenced in pharmaceutical drug dossiers as a critical regulatory requirement.

ibliographic References

[1] Varga B, Csonka Á, Csonka A, Molnár J, Amaral L, Spengler G. Possible Biological and Clinical Applications of Phenothiazines. *Anticancer Res*. 2017 Nov;37(11):5983–5993.
[2] Cookson J. Histamine in psychiatry: Promethazine as a sedative anticholinergic. *BJPsych Adv*. 2019;25:265–268.
[3] Howarth P, Hanuskova E, Plevkova J. Antihistamines in rhinoconjunctivitis. *Clin Allergy Immunol*. 2002;17:179–220.
[4] Babalola B, Malik M, Sharma L, Olowokere O, Folajimi O. Exploring the therapeutic potential of phenothiazine derivatives in medicinal chemistry. *Results Chem*. 2024 Jun;8:100123.
[5] Favre HA, Powell WH. *Nomenclature of Organic Chemistry: IUPAC Recommendations and Preferred Names 2013*. IUPAC Blue book.
[6] International Union of Pure and Applied Chemistry (IUPAC). [Internet]. Available from: https://iupac.org/.

How to cite this article:
Soufiane El Marrakchi et al. Jcpr.Human, 2025; Vol. 21 (7): 1-5

Conflict of Interest Statement:
The authors have no conflicts of interest to declare.