ECA 2021

sciforum

Conference Proceedings Paper

Action potential of aminonitriles in active sites of carbonic anhydrase isoforms

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Abstract Heterocyclic compounds have gained notoriety in the pharmaceutical universe after studies in numbers. Such compounds make the spectrum of action and development of countless drugs more flexible, and may become a viable alternative for, mainly, or antimicrobial development. In this perspective, the aminonitriles that lead the subgroup of notoriety in this advance are inserted, since, through their characteristic characteristics, an example of stability and resistance to hydrolysis, offers a forceful interaction with pathogens. Also, this relationship is closely related to enzymatic interactions of metabolic functioning, mainly not that it concerns the functioning of carbonic anhydrase and its isoforms. Given this, it is inferred to optimize and understand the bibliographic data already available to expand the field of compound actions, thereby characterizing the recognition of its possibilities for applicability in various pathologies.

Keywords: Aminonitriles; Bioactivity; Antimicrobial activity

Introduction

According to the advance of complications and worse recurrent degrees of pathologies not yet fully understood, the opportunity to develop studies that characterize substrates capable of developing possible alternative medications that can compose treatments today is enhanced. Heterocyclic compounds, such as aminonitriles, gain a prominent bias given recent studies made possible due to the exploratory potential of chemical compounds in this group, especially regarding the findings of the Strecker chemotype and its repercussions (1) (5).

In fact, aminonitriles are compounds of importance for the functionality of specifications, since they involve, in their composition, important chemical elements in the homeostasis of life, being these: nitrogen, carbon and hydrogen. In this perspective, the exploration and the possible use in the pharmaceutical industry are verified, since several reports already lead to the interpretation of potential explorations that concern the pharmacokinetic and pharmacodynamic characteristics of these compounds and how they interfere, in terms of a metabolic enzyme, in the functioning of numerous microorganisms (2).

Thus, such compounds make the understanding and potential of factors that can act from anticancer to antiviral, through antibiotics, antifungals and antibacterials, due to their versatility (2), their stability and their good resistance to hydrolysis (1). In this sense, the importance of the inhibitory relationship of carbonic anhydrase is codified, since there are correlations of interactions

between aminonitriles under study and the delaying mechanisms of microorganism homeostasis, such specification being acquired mainly due to its bipolarity (3).

For this reason, such compounds are found as an alternative for the development of other antimicrobials that mitigate complications, cause such microorganisms, since they involve a metabolic enzymatic component of a homeostatic character and can directly interfere with the maintenance and propagation of these organisms (6).

Materials and Methods

This work is characterized as an integrative bibliographic review with a qualitative and applied approach, aiming at understanding aminonitriles as a potential pharmacological component of medicines to expand the perceptions of the pharmaceutical industry.

In this context, the Biblioteca Virtual em Saúde (BVS) and PubMed databases were used to search for the objectified bibliographies. Then, to select the most appropriate descriptors for this study, a search was carried out on the DeCS (Descritores em Ciências da Saúde) database, with the most propitious: "aminonitriles", "mechanism" and "anhydrase carbonic" in the languages Portuguese, English and Spanish, in addition to the relevant synonyms. Also, for better formatting of the search formula, these descriptors were associated with Boolean operators ("AND", "OR" and parentheses).

The inclusion criteria were: studies that make the understanding of heterocyclic compounds more flexible, specifically aminonitriles, according to the mechanisms, as pharmacological potentials. In contrast, the exclusion criteria were: articles that addressed any heterocyclic compounds other than aminonitriles, as well as opinion articles, duplicate studies and articles that were not available in full.

Results and Discussion

Heterocyclic compounds, due to the existence of their chemical structure, gain space in viable chemical components to structure the functioning of new drug strands active in existing pathologies. This perception comes mainly from the development and understanding of aminonitrile chemotypes, characterized by being composed by the grouping of amines and nitriles, being, therefore, conditioned to contain important organoleptic properties for the handling of the compounds of numerous drugs, as predicted in its stability and strong resistance to hydrolysis (2).

Accordingly, studies condition a detail in this process of identification of such properties when correlated with the activation mechanism of these compounds made possible, mainly, by the occupation of active sites of important enzymes in the microorganism's homeostasis process, such as carbonic anhydrase (5).

The bipolar characteristic of these molecules under studies, like the aromatic sulfonamides that contain 1,3-oxazol-5-yl (5) and N-cyanosulfonamides (6), allows their actions in anhydrase type I and II isoforms. carbon (5) (6). As well as, studies also prove that Stecker chemotypes of aminonitriles conjugate this underlying information with isoforms I, II, IX and XII of carbonic anhydrase (1). In conjunction, some studies also report the performance of 1,2,4-oxadiazoles preferably in gram-positive, gram-negative bacteria and yeast-like fungi (8). Given this mechanism of reception of the active site and, consequently, the inhibition of standard homeostasis, aminonitriles permeate characteristic variations in temperature and concentration of the products and reagents involved in the reaction (5) to acquire such pharmaceutical potentialities, governed by the principle balance Le Chatelier, thus becoming a potential study for the composition of medicines.

In this context, carbonic anhydrase, which contains the main functionality of catalyzing the conversion process of carbon dioxide (CO2) and water (H2O) into carbonic acid (H2CO3), stands out in the prospect of maintaining the microorganism and, consequently, in the maintenance of pathologies that mainly involve cellular processes dependent on the concentration of anions and cations, such as *Streptococcus aureus, Escherichia coli, Salmonella Typhi and Candida albicans* (2).

It is also worth mentioning in this context that there are types of aminonitriles responsible for direct action in human carbonic anhydrase, being correlated with some pathologies, such as simple chronic glaucoma (4) and development of tumor masses (5). Also, it is worth emphasizing that,

possibly, they act in processes of systemic arterial hypertension (SAH), since acting directly as carbonic anhydrase inhibitors, consequently reduce the reabsorption of bicarbonate (HCO3-) together, through the flow antiport, sodium (Na+).

Therefore, it is necessary, in addition to developing further tests on these related benefits, to also highlight the character of consequences that arise from this use, such as the development of possible conditions unfavorable to the organism's homeostasis, such as metabolic acidity and hypokalemia.

Conclusions

Therefore, there is the availability of the development of studies that condition a broader understanding in view of the evidence already collected, since some trials have already proven aminonitriles as the potential for development and applicability in the pharmaceutical industry.

In the meantime, it is important to note that its applicability in the face of carbonic anhydrase is notorious mainly in the homeostasis of the balance between products and substrates involved in the carbon dioxide formation reaction.

Therefore, there is an urgent need to understand the benefits and harms involved in the development of possible alternatives that can make the expansion of alternative means more flexible for countless treatments.

Acknowledgements

The present work was carried out with the support of CNPq, National Council of Scientific and Technological Development - Brazil, through the Institutional Scientific Initiation Scholarship Program (PIBIC) – PIBIC/CNPq 2020/2021 and Voluntary Institutional Scientific Initiation Program (PIVIC) and of the Training Center for Teachers of the Federal University of Campina Grande (CFP/UFCG), campus of Cajazeiras-PB, Brazil.

References

1. Krasavin, Mikhail *et al.* "Further validation of strecker-type α-aminonitriles as a new class of potent human carbonic anhydrase II inhibitors: hit expansion within the public domain using differential scanning fluorimetry leads to chemotype refinement." **Journal of enzyme inhibition and medicinal chemistry** vol. 35,1 (2020): 165-171. doi:10.1080/14756366.2019.1693556
2. Shaikh, Irfan N *et al.* "Design, synthesis, and evaluation of new α-aminonitrile-based benzimidazole biomolecules as potent antimicrobial and antitubercular agents." **Archiv der Pharmazie** vol. 351,2 (2018): 10.1002/ardp.201700205. doi:10.1002/ardp.201700205
3. Krasavin, Mikhail *et al.* "Probing the 'bipolar' nature of the carbonic anhydrase active site: aromatic sulfonamides containing 1,3-oxazol-5-yl moiety as picomolar inhibitors of cytosolic CA I and CA II isoforms." **European journal of medicinal chemistry** vol. 101 (2015): 334-47. doi:10.1016/j.ejmech.2015.06.022
4. Supuran, C. T. Scozzafava, A.; Briganti, F. Carbonic Anhydrase Inhibitors: *N*-Cyanosulfonamides, a new Class of High Affinity Isozyme II and IV Inhibitors, **Journal of Enzyme Inhibition**, 14:4, 289-306, DOI: 10.3109/14756369909030323
5. Kouznetsov VV, Galvis CEP, Strecker reaction and α-amino nitriles: Recent advances in their chemistry, synthesis, and biological properties, **Tetrahedron** (2018), doi: 10.1016/ j.tet.2018.01.005
6. Ye, Wenyun *et al.* "Carbonic anhydrase II confers resistance to deltamethrin in Culex pipiens pallens." **Archives of insect biochemistry and physiology** vol. 96,4 (2017): 10.1002/arch.21428. doi:10.1002/arch.21428
7. Ayvaz, S. *et al.* "2-Amino-3-cyanopyridine derivatives as carbonic anhydrase inhibitors." **Journal of enzyme inhibition and medicinal chemistry** vol. 28,2 (2013): 305-10. doi:10.3109/14756366.2011.639016
8. Lopes, P. G. M.; Spader, T.; Alves, S. H.; Dornelles, L. Perspectivas sobre atividade antimicrobianas de compostos derivados 1,2,4-oxadiazólicos. **Saúde. Santa Maria**, v. 31, n. 1 e 2, p. 57-58, 2005.