EDITORIAL

Emerging Azoles: Structure Function Relationship and Their Therapeutic Potential

Natural Products Journal is one of the extremely important journals of Bentham Science Publishers. The current issue has been focused on to uncover many physico-chemical interactions persisting with regards to structural-function relationships of azole compounds and more importantly their therapeutic potential. Efforts have been made to find a link between natural and synthetic azoles' composition and structure with their physiological or therapeutic role through various articles contributed by diverse range of authors. Here is the brief summary of the articles:

Kim *et al*., emphasized upon Pyrazoline heterocycles which occupy a distinct attention in the field of synthetic and medicinal chemistry exhibiting a wide spectrum of biological activities including anti-inflammatory, anti-microbial, cytotoxic, anticonvulsant etc. [1-3]. Authors have made a sincere effort to review the synthetic and biological significance of Pyrazoline derivatives bringing together most of the recent studies.

Varughese *et al*., shed light on the broad-spectrum antimicrobial and therapeutic role of azole compounds in treating cancer linked fungal infections like candidiasis and aspergillosis. Authors have drawn comparisons between first First generation azoles with that of newer azoles in terms of their action potential and activity against resistant organisms. The role of azoles has been further extended to prostate cancer and breast cancer therapy through this article [4-6].

Sandhu *et al*., have shown promise in Azoles as effective antifungal agents. Authors are concerned about the growing resistance against azoles in fungal pathogens and side effects accompanied with the use of synthetic azoles which makes it necessary to search for some natural and effective azoles [6-10]. Authors have shown structure-function analysis of clinically important antifungal azoles derivatives through the collection of studies and also reviewed some important patents related to them.

Malik *et al*., mainly gained insight into the mechanistic preview as to how azole compounds bind to lanosterol 14α-demethylase and prevent the demethylation of lanosterol, thereby inhibitiing the fungal growth. Authors have focused their attention on antifungal potential of azole compounds with an emphasis on the corresponding drug resistance episode complemented with novel strategies for the development of new generation of azole compounds [11-14].

Gupta *et al*., reviewed the antimicrobial importance of natural imidazoles, their mode of actions and structure-activity relationship. The article would certainly help scientific community to bring further modifications or developments in the synthetic methodologies to biologically active compounds based on natural products containing imidazole moiety [15]. Thus natural imidazoles could be used as effective chemotherapeutics in future. Another article by Gupta *et al*., emphasized upon the effective use of second and third generation azole compounds against systemic fungal infections [16]. Given their toxicity profile being better than that of the first-generation triazoles and drug interactions remain manageable; these compounds represent a true expansion of antifungal arsenal for the future.

Kumar and Kaur emphasized upon the use of Triazoles and Oxadiazoles which are nitrogen and nitrogen-oxygen containing heterocycles, for the development of effective chemotherapeutic candidates. The article not only focuses on the biological importance of triazole and oxadiazole derivatives but also highlights synthetic pathways to achieve such compounds which would certainly help the scientific community to bring further developments in the isolation and synthetic methodologies for azole- based novel bioactive agents [17-21].

The continued success of the Journal is the result of a joint effort by a dedicated editorial team under the leadership of Dr. Naeem and we will continue to evolve progressively for the benefit of our contributors and readers. While thanking all the editorial members for their continued support and cohesive interactions, we reiterate our commitment for ethical and quality publications in frontier areas of Natural Product research. The lead guest editors and the executive editor would like to extend their gratitude to authors of this issue for their valuable scientific contributions. We simultaneously thank the valuable comments and suggestions of the reviewers to further improve the quality and scientific perspective of the articles. We eagerly look forward to receiving hot novel areas for contribution to The Natural Products Journal in future.

In the end, if you have any questions or suggestions to further improve the journal, please feel free to drop a line to the executive editor of NPJ.

REFERENCES

[1] Amir, M.; Kumar, S. Synthesis and anti-inflammatory, analgesic, ulcerogenic and lipid peroxidation activities of 3,5-dimethyl pyrazoles, 3-methyl pyrazol-5-ones and 3,5-disubstituted pyrazolines. *Ind. J. Chem*., **2005**, *44B*, 2532-2537.

[2] Palaska, E.; Aytemira, M.; Uzabay, I.T.; Erola, D. Syntheses and antidepressant activities of some 3,5-diphenyl-2-pyrazolines. *Eur. J. Med. Chem*., **2001**, *36*, 539-543.

[3] Bonesi, M.; Loizzo, M.R.; Statti, G.A.; Michel, S.; Tillequin, F. The synthesis and angiotensin converting anzyme (ACE) inhibitory activity of chalcones and pyrazoline derivatives. *Bioorg. Med. Chem. Lett*., **2010**, *20*, 1990-1993.

[4] Taplin, M.-E. Secondary hormone therapy for castration-resistant prostate cancer. *Oncology,* **2013**, *27*, 1-5.

[5] Bolden, J.E.; Peart. M.J.; Johnstone, R.W. Anticancer activities of histone deacetylase inhibitors. *Nat. Rev. Drug. Discov*., **2006**, *5*, 769-784.

[6] Greer, N.D.; Posaconazole (Noxafil): A new triazole antifungal agent. *Proc. (Bayl Univ Med Cent).,* **2007**, *20*, 188-196.

[7] Daniel, J.S.; Christopher, A.H; Carol, M.S. Current and emerging azole antifungal agents. *Clin. Microbiol. Rev.*, **1999**, *12*, 40-79.

[8] Eicher, T.; Hauptmann, S. The chemistry of heterocycles: Structure, reactions, synthesis, and applications, 2nd ed. John Wiley & Sons: USA **2003**.

[9] Hitchcock, C.A.; Whittle, P.J. Chemistry and mode of action of fluconazole. In cutaneous antifungal agents. eds Rippon, J.W. & Fromtling, RA. **1993**, pp 183-197. Marcel Dekker, Inc., New York.
[10] Information of recent patents on anti-fungalazole. Available at: http://www.google.co.in/#q=recent+patents+on+antifungal+azoles+compound (Accessed on: May 15, 2013).
[11] Ali, I.; Wani, W.A.; Khan, A., Haque, A.; Ahmad, A.; Saleem, K.; Manzoor, N. Synthesis and synergistic antifungal activities of a pyrazoline based ligand and its copper(II) and nickel(II) complexes with conventional antifungals. *Microb. Pathog.,* **2012**, *53*, 66-73.
[12] Kalamkar, V.; Joshi, M.; Borkar, V.; Srivastava, S.; Kanyalkar, M. Intermolecular interaction of voriconazole analogues with model membrane by DSC and NMR and their antifungal activity using NMR based metabolic profiling. *Bioorg. Med. Chem.*, **2013**, *21*, 6753-62.
[13] Aoyama, Y.; Yoshida, Y.; Sonoda,Y.; Sato, Y. Deformylation of 32-oxo-24,25-dihydrolanosterol by the purified cytochrome P-450_{14DM} (lanosterol 14α-demethylase) from yeast: Evidence confirming the intermediate step of lanosterol 14α-demethylation. *J. Biol. Chem*., **1989**, *264*, 18502-18505.
[14] Kanafani, Z. A.; Perfect, J.R. Resistance to antifungal agents: Mechanisms and clinical impact. *Clin. Infect. Dis.,* **2008**, *46*, 120-128.
[15] Jin, Z.; Muscarine, imidazole, oxazole and thiazole alkaloids. *J. Nat. Prod.*, **2003**, *20*, 584-605.
[16] Pasqualotto Pasqualotto, A.C.; Denning, D.W. New and emerging treatments for fungal infection. *J. Antimicrob. Chemother*., **2008**, *61*, l9-30.
[17] Butler, M.S. Natural products to drugs: Natural product derived compounds in clinical trials. *Nat. Prod. Rep.*, **2005**, *22*, 162-195.
[18] Kumar, V.; Kaur, K.; Gupta, G.K.; Sharma, A.K. Pyrazole containing natural products: Synthetic preview and biological significance. *Eur. J. Med. Chem.*, **2013**, *69*, 735-753.
[19] Kaur, K.; Kumar, V.; Sharma, A.K.; Gupta, G.K. Isoxazoline containing natural products as anticancer agents: A review. *Eur. J. Med. Chem.*, **2014**, *77*, 121-133.
[20] Kumar, V.; Kaur, K.; Gupta, G.K.; Kumar, S. Developments in synthesis of the anti-inflammatory drug celecoxib: A review. *Recent. Pat. Inflamm. Allergy Drug Discov*., **2013**, *7*, 124-134.
[21] Kumar, V.; Kaur K.; Karelia, D.N.; Beniwal, V.; Gupta, G.K.; Sharma, A.K.; Gupta, A.K. Synthesis and biological evaluation of some 2-(3,5-dimethyl-1H-pyrazol-1-yl)-1-arylethanones: Antibacterial, DNA photocleavage, and anticancer activities. *Eur. J. Med. Chem.,* **2014**, *81*, 267-276.

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