



SDI Review Form 1.6

Journal Name:	International Journal of Biochemistry Research & Review
Manuscript Number:	Ms_IJBCRR_24384
Title of the Manuscript:	Devastating impacts of 4-nonylphenol versus modulatory roles of novel thieno [2,3-c] pyrazole compounds in African catfish (<i>Clarias gariepinus</i>)
Type of the Article	

General guideline for Peer Review process:

This journal's peer review policy states that **NO** manuscript should be rejected only on the basis of '**lack of Novelty**', provided the manuscript is scientifically robust and technically sound.

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PART 1: Review Comments

	Reviewer's comment	Author's comment (if agreed with reviewer, correct the manuscript and highlight that part in the manuscript. It is mandatory that authors should write his/her feedback here)
Compulsory REVISION comments		
Minor REVISION comments	1- The commercial name and chemical structures of the present study materials? 2- Is it present in the fish environment ? How to reach to Clarias? 3- What is the lethal dose and optimum dose for Clarias 4- Is it toxic to offspring ?	Thank you for your useful suggestions. 1. There are no commercial names for these compounds simply because they are newly synthesized ones. For their detailed chemical structures, please see Table (1). 2. Pyrazole derivatives have been used as fungicides for treatment of fish mycoses (Häuser-Hahn et al., 2008). The wide application of some herbicidal and molluscicidal formulations, accidental sillage or discharge of untreated effluents into natural water ways contribute to long term exposure of non-target fish populations (El Shehry et al., 2010; Wu et al., 2012). This text was highlighted in the final manuscript in the introduction section. 3. Up to our knowledge, no available literature could be found concerning the lethal and most optimum doses of these compounds, but we found that the 96h LD50 of the most closely related compound (chlorantraniliprole) in fresh water fish Channa punctatus (Bloch) is 14.424 mg/L (Bantu and Vakita, 2013) which is indeed far away from our doses. Therefore, the examined doses



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		appear to completely safe especially when we take in consideration the complete absence of toxicological signs and behaviors along the entire course of our experiments. 4. Although some formula of pyrazole in the literature are known to disrupt the thyroid gland function in certain fish species (Raldúa et al., 2011). However, carbonitrile and carboxamide moieties, which had been used in the current study, have a broad spectrum of antioxidant activity exemplified on multiple levels. e.g. free radical scavenging, ferric ions reduction, metal chelating, superoxide anion generation, and lipid peroxidation (Ölgen et al., 2007; Saundane et al., 2013). So from a biochemical point of view, different substitution patterns in the pyrazole core resulted in wide physiological variations and changes in the benefit/risk outcomes. However, we frankly could not monitor their potential impacts on fish offspring. References: Bantu, N., Vakita, V.R., 2013. Acute toxicity of chlorantraniliprole to freshwater fish <i>Channa punctatus</i> (Bloch). <i>Advances in Zoology and Botany</i> 1, 78-82. El Shehry, M., Swellem, R., Abu-Bakr, S.M., El-Telbani, E., 2010. Synthesis and molluscicidal evaluation of some new pyrazole, isoxazole, pyridine, pyrimidine, 1, 4-thiazine and 1, 3, 4-thiadiazine derivatives incorporating benzofuran
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		moiety. European journal of medicinal chemistry 45, 4783-4787. Häuser-Hahn, I., Stenzel, K., Wachendorff-Neumann, U., 2008. Use of fungicides for the treatment of fish mycoses. Google Patents. Ölgen, S., Kiliç, Z., Ada, A.O., Çoban, T., 2007. Synthesis and evaluation of novel N-H and N-substituted indole-2-and 3-carboxamide derivatives as antioxidants agents. Journal of enzyme inhibition and medicinal chemistry 22, 457-462. Raldúa, D., Babin, P.J., Barata, C., Thienpont, B., 2011. Disrupting Effects of Single and Combined Emerging Pollutants on Thyroid Gland Function, Emerging Organic Contaminants and Human Health. Springer, 415-433. Saundane, A.R., Vijaykumar, K., Vaijinath, A.V., 2013. Synthesis of novel 2-amino-4-(5'-substituted 2'-phenyl-1H-indol-3'-yl)-6-aryl-4H-pyran-3-carbonitrile derivatives as antimicrobial and antioxidant agents. Bioorganic & medicinal chemistry letters 23, 1978-1984. Wu, H., Feng, J.-T., Lin, K.-C., Zhang, X., 2012. Synthesis and herbicidal activity of substituted pyrazole isothiocyanates. Molecules 17, 12187-12196.
<u>Optional/General</u> comments		