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Aflatoxin B_1: An Inactivation Proposal.

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Abstract: The effects of the high toxicity of most mycotoxins produced by *Aspergillus flavus* compared with the Aflatoxin B1 (AFB1) are negligible, thus depicting an alarming picture and reference potential for chemical study of a possible structural modification that establishes inactivation of toxicity and carcinogenic properties performed by AFB1. Therefore, we seek in this work a proposal for a chemical reaction to modify the toxicity of AFB1. Our study was based on the addition of acetyl radical due to Michael mechanism. In this perspective we conducted a study of quantum chemistry methods in the calculation of molecular parameters that indicate the feasibility of the proposed in humans and other animals.

Key-words: Aflatoxin B1, *A.flavus*, quantum chemistry
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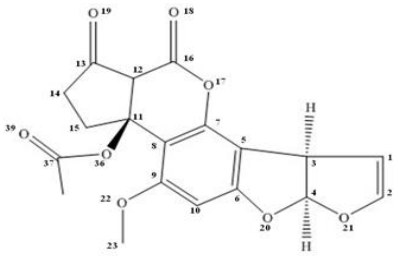
Introduction:
The fungi of the gender Aspergillus produce a varied number of toxins, however, a toxicity and carcinogenic power for AFB_1 that is about in 500 times greater in relation to others, being known as one of the natural product most carcinogenic[1]. In it's molecular structure AFB_1 has an lactone ring that is fundamental for it's chemical properties[2]. Our intention is to demonstrate the possible reaction of AFB_1 with acetic acid through the mechanism proposed (Michael Addition), mainly blocking the carcinogenic effect of AFB_1.

Methodology:
From the structures of the four possible isomers of AFB_1, we performed molecular mechanics (AMBER) and semi-empirical calculations AM1 and PM3 to reproduce the values obtained by Nicolás-vázquez et al. (2010)[2]. Once obtained the structures and the respective heat of formation, we start from the lower energy isomer to construct the possible structures resulting from a Michael addition of AFB_1 with acetic acid as in Figure 1. The structures obtained were also optimized with molecular mechanics (MM-AMBER) and Semi-Empirical (AM1 and PM3). To study the electronic structure of the compound, resulting from the addition of AFB_1 to acetic acid, we performed calculations using the Density Functional Theory (DFT) using the B3LYP Functional and 6-31 * G basis. In this work we made use of HyperChem 7.5 licensed to UFRPE.

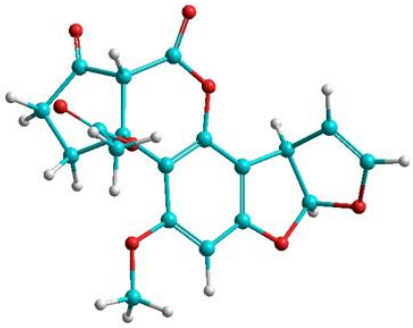
Figura 1: AFB1-Acetyl compound.



Results Obtained:

Fisrt we reproduced the structures of the isomers of AFB_1 with the same values of ΔHf for the four isomers with the semi-empirical method AM1 as obtained by Nicolás-vázquez et al. (2010)[2]. From the more stable structure, with the inclusion of the acetyl radical on the carbon atom 11 (Fig. 1) and the hydrogen atom on the carbon atom 12 considering all the possibilities as a consequence of the inclusion that can occur in cis and trans with respect to the principal plane of the molecule. Four structures are possible, that have been optimized with MM-ÂMBER, AM1 and PM3. One of the isomers (Fig. 2) showed the lowest ΔHf (-251,79 Kcal / mol) with PM3 Method, making it the most stable of the possible structures. With the same PM3, the ΔHf for the most stable isomer of AFB1 is -157.61 Kcal / mol. To complete our analysis, we obtain with PM3, the ΔHf equal to -100.63 Kcal / mol for acetic acid. The sum of the heat of formation of the reactants (AFB1 + Ac. Acet.) Gives -258.24 Kcal / mol. The product - reagent difference is around only 6.45 Kcal / mol. Considering that the molar mass of AFB_1 is 312 gr, this means that 1 mg of this compound would need only 0.02 calories, the amount of heat that could be supplied if we mixed the contaminated cereal with AFB_1 with a solution of acetic acid heated in Around 40 to 50 C. The amounts of aflatoxins found in contaminated products are of the order of micrograms, therefore, we would need much less heat for the reaction to happen. With the most probable AFB_1-Acetyl structure, we performed DFT calculations. The analysis of the results indicates that the inclusion of acetyl groups significantly alter the electronic structure in the lactone ring region when compared to AFB_1.

Fig. 2: More stable AFB1-Acetyl.



Conclusion:

Our results indicated the possibility of the reaction between AFB_1 and acetic acid through a Michael addition in heated medium with the temperature around 40-50 ºC. The calculations indicate that the electronic structure of the lactone ring of AFB1 is significantly altered, indicating change in the chemical behavior of AFB_1. The inclusion of the acetyl group makes the AFB_1 chain more ramified, which will prevent interaction with guanine in the DNA, avoiding its harmful effect on the DNA structure and possibly its carcinogenic effect[1]. This work continues with an achievement of the experimental stage in the attempt to verify what was indicated by calculations.

References:

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