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EPIMERIC INOSINE DERIVATIVES BY BIOCATALYSIS

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Introduction. Synthesis of nucleoside analogs using enzymes as catalyst whereas the result is an stero- and regioselective product offering better advantages comparing to traditional organic chemistry.
Biotransformation substrates, even using crude mixtures of enzymes result in a process environmentally friendly. The use of hydroxynitrile lyases from genus *Prunus*, have been established as an important source of this kind of enzymes (1).
The generation of a new chiral center in the synthesis of drug precursors is an important step in the strategy for preparing derivatives of nucleic acids, therefore, managing an easily accessible method to analyse the reaction products is one of the crucial stage in any process of synthesis.
Analysis of stereoisomers is not usually a complicated issue and can be carried out by HPLC either reverse or direct phase, however epimers are a kind of stereoisomer in which only one of the stereo-centre is different and is not sometimes obvious the necessity of chiral analysis system, in this work we compared Chiral HPLC and NMR studies in the analysis of a new chiral centre biocatalysed by oxynitrilases from several natural sources.

Methods: The biocatalysts were prepared as Solís *et al.* (2) as acetone dried powders from almond (*Prunus dulcis*), black cherry (*P. serotina var capuli*), cherry (*P. avium*), plum (*P. domestica*), guanabana (*Annona muricata*) and mamey (*Pouteria sapota*), were used without further purification. Solvents were HPLC grade purchased from Tecsiquim (México).
^{1}H NMR spectra were recorded on a Varian 400 MHz instrument, in $CDCl_3$; HPLC analysis were performed on an Agilent 1100 with a diode array detector, using a Chiracel OJ-H column.

Results: The biotransformation reaction is presented in the Figure 1 and the diasteromeric excess as well as conversion results are in the Table 1.

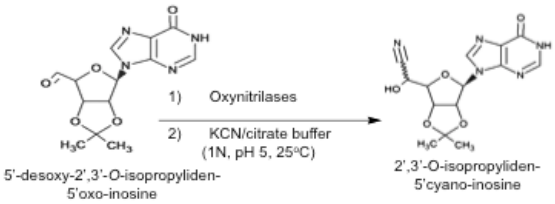

Fig.1 Inosine modification adding a new stereo-centre using hydroxynitrile lyases as biocatalysts from several natural sources.

Table 1. Diasteromeric excess of cyanohydrin inosine derivative in biphasic system at 20 °C, pH=5.

Enzyme source	Chiral-HPLC *de*%	^{1}H NMR *de*%	Conversion %
Almond	13.6	8.5	95-98
Black Cherry	12.9	14.7	89-94
Cherry	13.2	15.1	85-93
Plum	11.8	15.0	85-93
Apricot	10.0	17.2	93-96
Guanabana	9.9	12.0	86-92
Mamey	16.9	13.2	95-98

Conclusion: The best results were from mamey and cherry powders when used as a biocatalyst. The biotransformation could be further improved by changing pH and temperature conditions.

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References:

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