NANOASSEMBLIES: COVALENT DERIVATIVES OF NEVIRAPINE WITH POLYETHYNE GLYCOL DIACRYLATE

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INTRODUCTION

The design of nano-molecular transporters such as "hydrogels", based on PEG and chemically modified active compounds, significantly improves their hidrosolubilization.1 Considering that nevirapine (NVP) has proven highly effective in the highly active antiretroviral therapy (HAART), when used as first choice for the treatment of antiretroviral-naive patients, but has low aqueous solubility, investigation about its improvement is necessary.

RESULTS AND DISCUSSION

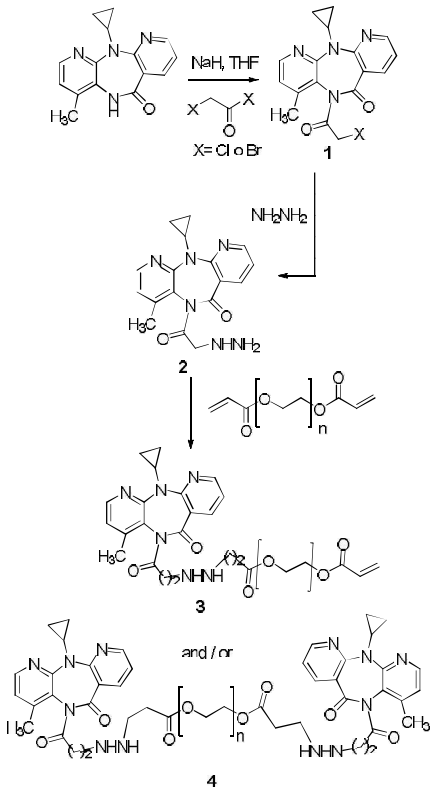
Within the scope of our research in this area, we developed the synthesis of modified NVP through the covalent union with PEG derivatives. The chemical synthesis and characterization of conjugates of NVP with hydroxylated polymers was studied using different synthetic routes for the subsequent antiviral activity evaluation of the resultant conjugates.

The NVP was isolated from commercially available medicaments. After of assay several reaction conditions in the presence of different bases and alkylating or acylating reagents, the incorporation of an α-haloacyl moiety (bromoacetyl, chloroacetyl or β-chloropropionyl) on the lactam nitrogen atom to obtain product **1**, was successfully achieved.

Then, different reaction conditions were tested over the chloro or bromo atom of the α-haloacyl derivatives **1** for its nucleophilic substitution by hydrazine, silver nitrate or HMTA to obtain derivatives such as **2**. The scheme (Scheme 1) shows the synthetic sequence employing hydrazine to obtain the corresponding derivative **2** and the reaction of nucleophilic addition with polyethylene glycol diacrylate on it to afford **3** and/or **4**, currently in study.

CONCLUSION

From the research carried out has succeeded preparing NVP derivatives to improve hydrosolubility characteristics of that drug by the covalent attachment with PEG derivatives. For that, some suitably substituted synthetic intermediates had been prepared and fully characterized.



Scheme 1

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