Originating from America and introduced a few centuries ago in Europe, *Xanthium macrocarpum* DC. (Asteraceae) also called „Lampourde à gros fruits“ is a species commonly growing on the edges of the Loire. Xanthanolides (sesquiterpene lactones) found in this plant exhibit interesting biological activities [1]. These activities are usually explained by their alkylating properties due to the presence of the α-methylene-γ-lactone function which is also related to the toxicity of several plants. As recent reports pointed out the potential of dimeric or monomeric sesquiterpene lactones as farnesyltransferase (PFTase) inhibitors, we decided to explore this activity knowing that PFTase is an interesting target to find new effective therapeutic agents for the treatment of cancer. So, the objective was to obtained atoxic hemisynthetic derivates from the natural xanthanolides: xanthatin and xanthinin. These compounds were first isolated in one step from the crude chloroformic extract of the leaves of *X. macrocarpum* using different methods of chromatography: silica gel and a 5L pilot scale FCPC® (Fast Centrifugal Partition Chromatograph, Kromaton, Angers, France). We have shown that FCPC® is more efficient for purification: solvent consumption is lowered (divided by 2), with highest purity (5 fold increase on average), high loading capacity (2g of extract/L of organic solvent), and manipulation time reduction (few hours versus few days) [2]. Sixteen derivates were investigated as potent inhibitors of protein farnesyl transferase. These results showed that the α-methylene-γ-lactone function is not required to insure a PFTase inhibitory activity whereas the α-methyl-γ-lactone function is responsible for a non competitive-inhibition.
Liens


Publié sur Okina (http://okina.univ-angers.fr)