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How the presence of metal atoms and clusters can modify the properties of Silybin? A computational prediction

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ABSTRACT

Silybin and de-protonated silybin are well-known antiradical molecules. The interaction of these two molecules with metal atoms and clusters (tetramers) of Cu, Ag and Au may modify chemical properties. In this report, systems containing metal atoms and clusters (neutral and cationic systems) interacting with silybin and de-protonated silybin are analyzed, by applying Density Functional Theory (DFT) calculations. In order to explore changes in reactivity due to the presence of metals, the free radical scavenging properties of these new systems were studied by analyzing the electron transfer mechanism. Reactivity was also studied by considering the Molecular Electrostatic Potential maps of the most stable systems. Raman spectra were also obtained, both with and without metals. As apparent in this report, electron donor-acceptor capacity is improved with the presence of metals, and the presence of Cu, Ag and Au (atoms and clusters) considerably increases signals from the Raman spectra, which may be useful for experimental detection. The conclusion derived from this study is that the presence of metals not only enhances characterization signals but also modifies electron donor acceptor capacity.

1. Introduction

Silybum marianum (milk thistle) is a medicinal plant that has received tremendous attention during the last decade due to new and emerging applications in medicine and also as a herbal remedy for liver treatment [1–8]. The useful extract from this plant is named silymarin [4], and comprises a natural mixture with beneficial properties for health, specifically related to its hepatoprotective and antiradical characteristics. In previous reports, [9] theoretical studies of the major components of silymarin indicate that, although all components of silymarin have peculiar properties, none of the compounds being studied registered outstanding antiradical capacity compared to the others. In this sense, silymarin is an interesting mixture with antiradical properties and we now know that all components studied present similar chemical properties [9].

The main component of silymarin is silybin (SIL) [3,4]. Silybin is a mixture of two diastereomers: silybin A and silybin B, being silybin B the most abundant in nature. SIL is a molecule with important antiradical properties [9–20]. The antiradical properties of SIL are considered to be responsible for its protective actions. SIL is currently used as an active component in many dietary supplements, cosmetics and dermatological preparations. Studies have also considered the phototoxic potential of the main components of silymarin, however no phototoxicity was revealed for these compounds [21]. It has been suggested that SIL is a potential cancer preventive substance with multifactorial components that manifest anti-cancerogenic activities [22,23]. All these beneficial properties for health are apparently related to its strong antiradical activity. Previous investigations have focused on the antiradical properties of SIL; both theoretical and experimental [24–26]. Electron transfer is one of the reaction mechanisms that is important to analyze. This mechanism measures the capacity of an antiradical molecule to either donate or accept electrons in order to stabilize free radicals.

Antiradical properties of organic molecules change due to the interaction with transition metals [27]. In previous theoretical reports, it was shown that astaxanthin interacts with transition metals such as Cu and Cd [28]. This interaction between astaxanthin and metals modifies antiradical properties and makes the compounds redder in colour. In a subsequent investigation with shrimps, it was demonstrated that shrimps living in water with traces of copper became redder than those living in pure water [29]. Shrimps contain astaxanthin and although it is not possible to say that the change in colour is due to the interaction of astaxanthin and copper, it is a fact that the presence of copper modifies

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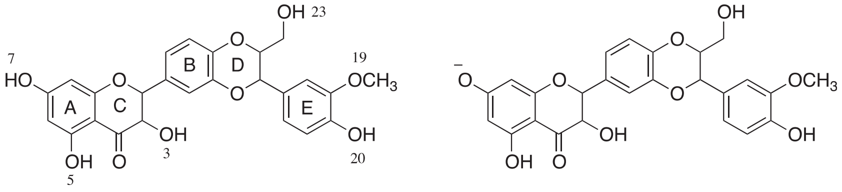

Fig. 1. Silybin (SIL) and de-protonated silybin ($[\text{SIL}_{(\text{-H})}]^{-1}$).

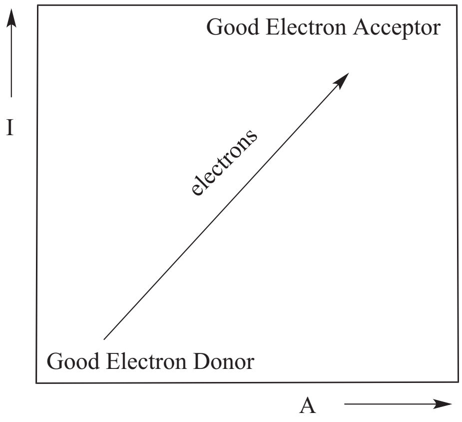

Fig. 2. Full electron donor-acceptor map.

the colour and chemical properties. Astaxanthin's ability to interact with metals is not unique. SIL is capable of interact with transition metals such as Cu^{2+} to produce a complex that has pro-oxidant properties [24–26]. Although all results indicate the antiradical properties of SIL, there are no theoretical investigations that analyze the interaction of SIL with transition metal atoms and clusters. It is however essential to discern how the presence of metal atoms and clusters can modify reactivity, because metals may increase their therapeutic capacity or modify properties so that substances no longer function as possible drugs.

It is well known that the interaction between organic molecules and transition metals increases the possibility of detecting single molecules in solution. Surface-Enhanced Raman Scattering (SERS) [30–32] represents a useful technique resulting in strongly increased Raman signals from molecules, which have been attached to metallic structures. Due to their localized surface plasmon resonance, gold, silver and copper are commonly used to

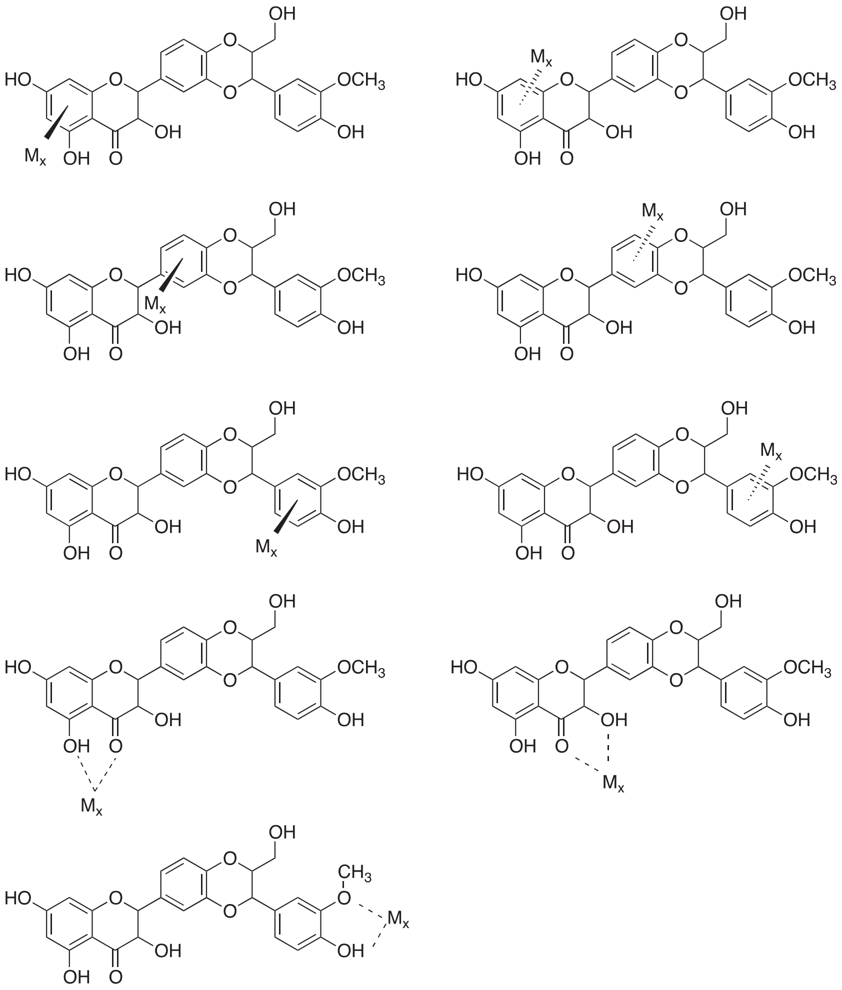

Fig. 3. Schematic representation of the initial geometries for SIL interacting with metal atoms and clusters (neutral and cationic systems). (M is Cu, Ag or Au; x is 1 or 4).