IN SILICO MEDICINAL CHEMISTRY AND PHARMACOLOGY OF NATURAL PRODUCTS: UNDERSTANDING BIOLOGICAL EFFECTS THROUGH MOLECULAR MODELLING AND MOLECULAR DYNAMICS SIMULATIONS

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Several important aspects of the chemistry and pharmacology of natural products are amenable to being studied by the same computational tools that are used in the case of synthetic compounds: from calculation of structures and chemical reactivity to ligand docking and structure-activity relationships. A variety of examples will illustrate the characterization of ligand-binding sites in proteins [1,2], the docking of small molecules into protein binding sites [1,2], the covalent and non-covalent binding of antitumor agents to DNA in a sequence-selective fashion [3-6], as well as the importance of molecular dynamics in the simulation of conformational changes [1,2] and in the determination of binding free energy differences [6,7]. The results obtained using these methodologies yield information that sometimes is beyond current experimental possibilities and can be used as a guide in the selection of experiments. On the basis of our improved level of understanding of molecular recognition, the widespread availability of target structures, and the ever-increasing power of computers, it is reasonable to assume that *in silico* methodologies will continue to aid in the interdisciplinary work aimed at the design and optimisation of new drugs.

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