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Bisphosphonates (BPs) are a class of drugs widely used in the treatment of several metabolic bone disorders associated with increased bone resorption, including osteoporosis, Paget’s disease and metastatic bone disease [1-3]. Although BPs can directly inhibit the cellular activity of osteoclasts, their ability to adsorb to bone mineral is also an important factor in determining their potency and duration of action [4]. In this study, we performed a molecular modelling analysis, by molecular mechanics [5], of the molecular structures of hydroxy(1H-indazol-3-yl)methylene-diphosphonic acid (BP1; Figure 1a) and hydroxy(1-methyl-1H-indazol-3-yl)methylene-diphosphonic acid (BP2; Figure 1b) and examined their interactions with hydroxyapatite by energy-minimising 50 different orientations for judiciously selected low energy conformers of each ligand at 10 Å from the mineral surface. Their interaction energy suggests that BP2 interacts stronger with hydroxyapatite than BP1. These results are in agreement with in vitro and in vivo studies of the 153Sm-BPs complexes. Complex 153Sm-BP2 showed, in vitro, higher HA binding than complex 153Sm-BP1. In vivo studies showed different pharmacokinetics parameters with complex 153Sm-BP2 presenting initial higher levels of bone uptake than complex 153Sm-BP1, which concentration is increasing during the 24 h period studied [6].

![Figure 1](image)

**Figure 1** – a) hydroxy(1H-indazol-3-yl)methylene-diphosphonic acid – BP1; b) hydroxy(1-methyl-1H-indazol-3-yl)methylene-diphosphonic acid – BP2.

**References**


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