INDOLO[2,3-B]QUINOLINE DERIVATIVES AS NOVEL PROMISING ANTITUMOR AGENTS.

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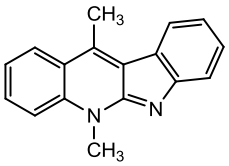
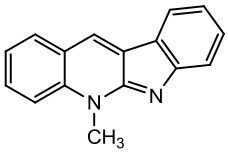
In the search for novel antineoplastic compounds we have found that four-membered, linear 5,11-dimethyl -5*H*-indolo[2,3-b]quinoline (DIMIQ) (**1**) reveals cytostatic activity *in vitro* and moderate antitumor activity *in vivo* in mice melanoma B16 as well as leukemias L1210 and P388 [1]. Preliminary studies showed that DIMIQ stabilizes DNA-topoisomerase II complex [2]. Some years later indolo[2,3-b]quinoline was found as an alkaloid *neocryptolepine* (**2**) in the West African shrub *Cryptolepis sanguinolenta* [3].

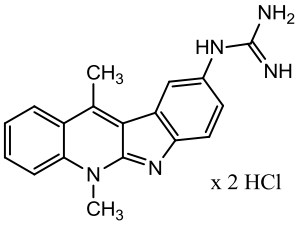
Unfortunately, DIMIQ's high toxicity, lack of selectivity and very low solubility in aqueous media seriously limit the practical use of this compound as an anticancer drug. Extensive research on the structure-activity relationships of different indolo[2,3-b]quinoline derivatives showed that the position and type of the substituent is conclusive both to the antitumor activity and general toxicity of the compound. These studies led us to discover derivatives of DIMIQ which exhibit very low toxicity against normal cells and are highly toxic against selected human tumors (e.g. **3**) [4]. These derivatives are soluble in water and some of them are able to overcome multidrug resistance in human tumors cells.[5]



1. DIMIQ



2. Neocryptolepine



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