NATURAL AND SEMISYNTHETIC ANTRAQUINONES, FLAVONOIDS AND NAPHTOQUINONES EFFECTS ON CELL CYCLE IN HUMAN OVARIAN CANCER

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Increasing epidemiological and experimental evidences indicate that natural polyphenols are interesting substances in chemoprevention, a new approach to develop efficient strategies of controlling cancer (1). We studied the effect of rhein (antraquinone), quercetin (flavonoid) and plumbagin (naphtoquinone) on wild type (2008) human ovarian carcinoma cells and on cis-platin (CDDP) resistant variant (C13). Cells were treated for 24 hours with (0.1mM-0.1mM) of different natural phenols and cytotoxicity and cell cycle were measured. Results demonstrated that all substances were cytotoxic at micromolar concentration, also causing evident alterations of cell cycle phases and apoptosis. In order to test the likely mechanism of inhibition of cell cycle by natural phenols an hightroughput consensus docking study with ATP-binding pocket of protein kinase was performed. Results indicated some small derivatives of antraquinones, flavonoids and naphtoquinones with likely improved affinity for ATP-binding. These derivatives were synthetized and their effects atconcentrations (0.1mM-0.1mM) were assayed on carcinoma cells. Results showed that semisynthetic naphtaquinone were more potent than antraquinones and flavonoid derivatives to cause cytotoxicity and cell cycle alterations.
Our data showed that natural phenols may be considered chemosensitizing cytotoxic substances (2) and also that more selective targeted compounds in cancer may derive from in silico design of phenols derivatives.

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2. Howells LM, Manson MM. Prospects for plant-derived chemopreventive agents exhibiting multiple mechanisms of action. Curr Med Chem Anticancer Agents. 2005, 5:201-13.