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Design, synthesis and structure-activity relationship of novel semi-synthetic flavonoids as antiproliferative agents

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Naturally occurring flavonoids have elicited a proven role as capacity having agents for the management of cancer. Thus, this research deals with the design and synthesis of semisynthetic flavonoid scaffold based derivatives viz., furochalcones (3a-e, 6a-d and 9a-d), furoflavones (10a-d, 11a-d, 12a-d, 18a&b), flavones (21a-d), furoaurones (13a,b, 14a-d and 15a-d) and 7-styrylfurochromones (22a-d and 25a-e). The novel compounds were evaluated for their antiproliferative activity against a panel of 60 cancer cell lines comprising 9 types of tumors. Ten compounds belonging to the major subgroups of flavonoids viz., furochalcones (3a, 3d, 6b, 9a and 9b), furoflavones (12a and 12c), furoaurones (15d), styrylfurochromones (25b and 25e) showed very promising activity. These active compounds were also evaluated *in vitro* as kinase inhibitors against CDK2/cyclin E1, CDK4/cyclin D1 and GSK-3 β and the best inhibition was displayed against GSK-3 β with the allylfurochalcone derivative 9b exhibiting 80% decrease in GSK-3 β catalytic activity. On the other hand, the styrylfurochromone 25e interestingly showed a 13% enhancement of GSK-3 β catalytic power and a 12% reduction in CDK4/cyclinD1 activity. Finally, the *in vivo* anti-tumor activity of 25e was evaluated against breast cancer induced in mice. The results showed a profound anti-tumor effect of 25e that accompanies a significant increase and decrease in the levels of GSK-3 β and cyclin D1, respectively.

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Fabrication and characterization of poly [N-isopropylacrylamide-co-allyl glycidyl/iminodiacetic] grafted to magnetic nano-particles for the determination and extraction of famotidine in biological samples

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A novel method is reported for grafting of poly [N-isopropylacrylamide-co-allyl glycidyl/iminodiacetic] based on iron oxide nano-particles modified by 3-mercaptopropyltrimethoxysilane. The grafted nano-polymer was characterized by elemental analysis, Fourier transform infrared spectroscopy, thermogravimetric analysis, transmission electron microscopy and scanning electron microscopy. The analytical parameters such as pH, temperature and contact time of the grafted nano-polymer were studied. Determination and extraction of famotidine in human biological fluids were evaluated with high great accessibility to the active sites in the grafted sorbent. The equilibrium adsorption data of famotidine by grafted nano-sorbent were analyzed by Langmuir and Freundlich models. The sorption capacity of the nano-sorbent was 116 mg.g⁻¹ at an optimum pH of 7. Almost 73% of famotidine was released in simulated gastric fluid in 1 h and 70% was released in simulated intestinal fluids in 30 h at 37 °C. These results show that this new magnetic grafted nano-polymer is adequate for enteric drug delivery. The suitable cause for choosing this particular polymer was its strong retention and subsequently longer controlled release for drug delivery. In other investigation, the effect of temperature on famotidine release was evaluated. The sorption and desorption studies were carried out at five temperatures (25-45 °C). The results showed that the maximum adsorption of famotidine occurred at 30 °C. Because, at low temperatures, the repeating chains of N-isopropylacrylamide on the nano-sorbent were in expanded form and famotidine better loaded onto the sorbent. At high temperature the grafted polymer containing the thermo-sensitive monomer shrank, so the release of famotidine increased.

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