

## Biological activity of hydantoin derivatives on efflux pump systems of bacteria and cancer cells

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Hydantoin derivatives possess a variety of biochemical and pharmacological properties and are used to treat many human diseases. They possess good anticonvulsant properties and depending on the nature of substitution on the hydantoin ring, a wide range of other pharmacological properties, e.g., fungicidal, herbicidal, antitumor, anti-inflammatory, anti-HIV, hypolipidemic, antiarrhythmic and antihypertensive activities, have also been identified. Although hydantoin compounds are studied extensively, there are not many studies to investigate their anticancer properties.

In the present study, thirty hydantoin compounds were evaluated for their efflux modulating effects in bacteria and cancer cells using fluorescence activated cell sorting and real-time fluorimetry. The modification of intracellular drug accumulation was evaluated by flow cytometry using rhodamine 123 accumulation assay and real-time fluorimetry based on the intracellular accumulation of ethidium bromide.

Among the hydantoin derivatives tested as potential efflux pump inhibitors, compound AD-29 showed potent efflux modulating activity in bacteria and cancer cells as well. We have demonstrated that some hydantoin derivatives have efflux modulating effects in bacteria; however, they do not have antibacterial activity.

In cancer cells, compounds SZ-7, LL-9, BS-1, MN-3, P3, RW-15b, AD-26, RW-13, AD-29 and KF-2 significantly increased the retention of rhodamine 123 and the most effective compounds were BS-1, MN-3 and JH-63 at the lowest concentration studied (4 µg/mL). The use of the EB fluorimetric method correlated well with those obtained from flow cytometry.

Based on these results we are planning further *in vitro* and *in vivo* experiments to study the possible applications of hydantoin derivatives in antibacterial and anticancer chemotherapy.