CONCLUSIONS
Our studies on effects of cisplatin on Dictyostelium discoideum indicate that both the phases of its life cycle i.e. growth and development are effected by the drug.

Our experiments on the growth phase encompass a wide array of events ranging from cell survival to folic acid chemotaxis, endocytosis, macromolecular synthesis etc. The cytotoxic nature of the drug is established by the decrease in surviving fraction of the cells after they had been exposed to cisplatin. The drug is known to mediate its cytotoxic effects by interfering with the DNA replication machinery. This is supported by our experiments on DNA synthesis which showed an inhibition in the incorporation of $^3$H-thymidine, thereby indicating an inhibition of DNA replication. Cisplatin does so by forming adducts with DNA bases.

Other parameters of growth viz. germination of spores, morphology of the colonies formed by the cells, folic acid chemotaxis, process of endocytosis, were inhibited to different extents depending on the dose and duration of cisplatin treatment. Of the above mentioned events, germination of spores requires the synthesis of a new set of proteins and the remaining events, in addition to protein synthesis, also require a dynamic cell membrane. We monitored the incorporation of $^3$H-leucine in cisplatin treated cells and found a net decrease in synthesis as
compared to the control cells. SDS-PAGE analysis of cytoskeletal proteins revealed an altered profile of actin and myosin amounts. Cisplatin treatment has been reported to disrupt microtubules and microfilaments. In addition, cisplatin efficiently crosslinks the sulfhydryl rich groups in membrane proteins. The net result of all these effects is functional and structural damage of the membrane resulting in the impairment of various membrane related events, viz., endocytosis and chemotaxis.

Development of *Dictyostelium discoideum* cells also requires an active role of membranes to mediate cell streaming, cell-cell adhesion, cell sorting etc. In our experiments, where the cells which had been treated with cisplatin during growth phase were allowed to develop, the effect of the drug appears to persist. Treated cells show alteration in individual steps of development as well as overall morphogenesis. cAMP chemotaxis and ePDE activities were severely effected and from streaming stage onwards there is a rapid synchronous development till culmination. Also, the fruiting bodies formed at culmination appeared to have altered proportions of spore and stalk cells. This indicates an underlying mechanism by which cisplatin influences various signalling pathways of development.

*Dictyostelium discoideum* cells treated with cisplatin shows a number of morphological artifacts. These include hypervacuolation, membrane blebbing and pinching off,
membrane rufflings, bi- and multinuclear conditions. These effects are probably due to the action of drug on the membrane and underlying cytoskeleton as well as its effect on mitochondria, E.R and Golgi etc.

From our studies it is evident that effects caused by cisplatin are very clearly manifested in Dictyostelium discoideum cells. Various morphological, biochemical as well as developmental deviations from the normal course can be qualitatively as well as quantitatively recorded. In addition, most of the assays are simple to perform and give results in less than 24 hrs. Thus, Dictyostelium discoideum may serve as a model system for testing the toxicity of a given chemical.