Review of Literature
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The crude drug Plumbago zeylanica and Plumbago rosea are extensively used in traditional systems of medicine practised in India. It is used as an anticancer drug in Siddha system of medicine (Mudaliar, 1964). Earlier work in Captain Srinivas Murthi Drug Research Institute for Ayurveda, Madras as well as in the National cancer Institute, Bethesda, Maryland, USA, have indicated that certain naphthoquinones like lapachol is associated with tremendous biological activity, viz anticancer and antimalarial.

Administration:

LD₅₀ of plumbagin is found to be almost 16mg/kg body weight orally and intraperitoneally in mice (Mohana Krishnaswamy and Purushothaman, 1980). According to Debray et al (1973), the LD₅₀ value of plumbagin, when given intraperitoneally to mice was found to be 15 mg/kg body weight.

ED₅₀ of plumbagin in rats is found to be 2mg/kg body weight (N.C.I.Bethesda). ED₅₀ of plumbagin for fibrosarcoma in rats is found to be 0.75mg/kg body weight (Mohana Krishnaswamy & Purushothaman, 1980).
The mode of administration of plumbagin was by ip route (intraperitoneally) or orally, the vehicle used was olive oil or propylene glycol (Mohana Krishnaswamy & Purushothaman, 1980).

Antitumour properties:

Methyl cholangthrene induced fibrosarcoma in rats is used for the primary screening of potential anticancer drugs. Plumbagin possesses antitumour activity against this fibrosarcoma in Wistar strain of rats (Krishnaswamy and Purushothaman, 1980), when given intratumour and orally at 2 mg/kg body weight, the tumour shows 70% and 60% regression respectively. Plumbagin was also tested against P388 lymphocytic leukemia and L1210 lymphoid leukemia at the dosage 4mg/kg body weight at The National Cancer Institute, Bethesda, USA. Chandrasekaran and Nagarajan, 1983 assessed the growth inhibitory effect of plumbagin against fibrosarcoma in Wistar strain of rats. Plumbagin at a dose of 10 mg resulted in 75% regression in tumour growth. Pretreatment with plumbagin had no effect on the time of onset of tumour in rats.
Antibacterial Properties:

It shows antibacterial activity against Staphylococcus aureus and E. coli, (De Saint Rat et al., 1946). Its activity against Mycobacterium tuberculosis (H37 RVs and Human T.B) has been shown by Rao and Seshadri, 1955. In 1956, Atkinson showed the strong antibacterial activity of Plumbago zeylanica. That the root extract of Plumbago showed antibacterial activity against Bacillus mycoides, B. pumilis and B. subtilis was shown by De Lima (1967). Mukharya and Dahia, 1977 showed its activity against Salmonella typhi, S. paratyphi, Sarcina lutea, Xanthomonas citri, X. malvacearum. Plumbagin inhibits the growth of both gram positive and gram negative bacteria.

Staphylococcus citreus, Staph aureus, Staph albus, Sal. paratyphi, S. dublin, Corn equi and Kleb. pneumoniae are inhibited at 20 µg/ml (Mohana Krishnaswamy & Purushothaman, 1980).

Antifungal properties:

Activity of plumbagin at different pH against various fungi was studied by Amondikar (1974). He found that, it is more active at neutral pH against S. albus ATCC-12228, V. cholerae – 9459. It shows antifungal activity at 10 ug/ml against Rh. nigricans, E. floccosum, M. nana, P. notatum, P. canadense (Mohana Krishnaswamy & Purushothaman, 1980).
Abortifacient properties:

Its abortifacient activity was first reported by Nadkarni & Nadkarni in 1954. Bhatia & Lai (1933) have reported it to be a powerful irritant to smooth muscles and uterus. When applied on uteri, it causes abortion (Kirtikar & Basu, 1973). When given orally at 1mg/kg it causes antiimplantation effect and abortion in albino rats without teratogenic effects. Antiovulatory effects were seen in rabbits treated with 1.0 mg/kg body weight of plumbagin (Premakumari et al., 1977) Petroleum ether extract, alcoholic extract and aqueous extracts of Plumbago zeylanica failed to show any anti-implantation activity (Saksena et al., 1970). But, in contrast to this earlier finding, Gupta & co-workers, 1971 and Mahli and Trivedi, 1972 have reported the 100% anti-implantation effects of plumbagin in 50% alcoholic extracts of P. zeylanica. Chowdury et al., (1982) also reported the anti-fertility activity of P. zeylanica.

Anti-coagulatory effect:

An oral administration, at 1mg/100g body weight of plumbagin administrated orally caused a significant increase in prothrombin time, SGPT and alkaline phosphatase levels in liver tissue & decreased SGPT levels in serum (Santhakumari & Rathinam, 1978).
Effect on microbial Enzymes:

In 1974, Blagonrarova and Sheherbanovskii investigated the effect of natural & synthesised naphthoquinones on some important enzyme systems of microbes and higher plants. They reported the stimulation of peroxidase activity by plumbagin, in many of the systems studied.

Mutagenic properties:

It was shown to be mutagenic in strain TA 2637 of Sal. typhimurium (Tikkanen et al., 1983)

Effect on cell growth & mitosis:

It exhibited mitotic arrest, chromosomal changes like polyploidy, micronucleus, anaphase bridges, giant cells, stickiness & lagging of chromosomes, reduction of mitotic index and restitution at metaphase in chick embryo fibroblasts. At higher concentrations it resulted in nuclear and cytoplasmic vacuolization and nuclear polymorphism (Santhakumari et al., 1980)

Effect on cellular physiology:

Plumbagin produces mitodepressive effect which is clearly demonstrated in the root tips of Allium cepa in cultured human lymphocytes. In mouse with the
increase of duration an increase in mitotic reduction was observed. This could probably indicate the latent effect of plumbagin (Kihlman, 1966). In mice, the effects of plumbagin seems to be duration dependent. A decrease in the mitotic activity in bone marrow was observed at 48h at a dose, 0.00375g/kg body weight. In Syrian hamsters, no consistent effect on mitotic index in bone marrow could be discerned. A reduction in the mitotic activity was seen at the highest concentration and there was an increase in the mitotic activity at doses 0.00375 and 0.0075g/kg body weight, (Santhiya, 1983).

In lymphocytes, on continuous exposure the reduction in mitotic activity was dose dependent. However exposures to plumbagin at various intervals of the culture period showed an increase in mitotic activity at an exposure period of 32 - 48h of culture growth.

In general, a reduction in mitotic activity due to plumbagin was evident in all the test systems. A number of factors have been found to be responsible for the chemically induced inhibition of mitosis (Deysson, 1968).

Since the naphthoquinones & their derivatives are known to be strong inhibitors of mitosis they inhibit several enzyme reactions and most action with sulfhydryl
group (SH) indispensable for the functioning of enzymes and structural proteins (Bieseke, 1958, Hoffman-Ostenhof, 1963). It is well known that protein and sulphur metabolism is of utmost importance in growth and cell division and evidently substances blocking SH groups, have a marked effect upon the dividing cell (Kihlman, 1966). Derivatives of naphthoquinones interact with the proteins and they inhibit enzymatic reactions in the oxidation of SH group (Fieser and Fieser, 1956).

A susceptibility to the inhibition of DNA and RNA synthesis by benzo and naphthoquinones has been reported by Lin et al., 1973.

They synthesized a number of naphthoquinone derivatives for their biochemical and antitumour activity against in vitro tumour systems (755 Adenocarcinoma and Sarcoma 180). These quinone derivatives were found to inhibit the synthesis of both DNA and RNA.

Quinones and their derivatives are known to participate in oxidation-reduction reactions of mitochondria, chloroplasts and chromatophore fragments. Substances which inhibit oxidative phosphorylation are known to inhibit cell division (Kihlman, 1966). According to Epel (1963) an inhibition of oxidative
phosphorylation reduces the level of ATP. More than 50% reduction of ATP level results in the complete inhibition of mitosis. It has been postulated that D-Guinone methides act as intermediates in oxidative phosphorylation. Therefore, it seems that there are 2 possibilities by which plumbagin could inhibit cell division either by inhibiting DNA synthesis or by participating in oxidative phosphorylation.

All cytotoxic drugs with antitumour activity probably reveal or express their effects by impairing the synthesis or function of nucleic acids which are closely involved in the processes of cell division (Wilson, 1973).

Metabolism of Plumbagin:

Plumbagin in rats given 1.6mg/0.2 ml could be detected in blood upto 24hrs. Except for the 1st 2h urine, all other samples showed plumbagin. The major proportion being excreted at 24 h with traces at 48 hrs of urine sample. Considerable amount of plumbagin was also excreted in the faeces (Chandrasekaran and Nagarajan, 1981).