The present study has shown that the SLNs being a versatile technology have the potential to improve the biopharmaceutics properties of AD and open up new perspectives for the formulation of poorly soluble drugs. The SLN approach was used in an attempt to increase its bioavailability. An optimized AD-SLN was prepared, using two lipids cetyl alcohol and gelucire 50/13, with 0.2% tween 80 as surfactant, and 0.2 % PVA as stabilizer in distilled water as an aqueous phase. The AD-SLN was optimized on the basis of lower particle size, minimum polydispersity index, sustained drug release from SLN, lower surfactant concentration, higher solubilization of drug in the minimum amount of lipid as well as higher bioavailability. Due to entrapment of AD into SLN, it permits controlled rate of drug release and showed a sustained release effect of AD. The results proved that the AD-SLNs produced by solvent injection method, using cetyl alcohol as a lipid, are more effective than the AD-SLNs prepared by gelucire 50/13.

The bioanalytical method was developed and validated in accordance with FDA criteria. The assay achieved good sensitivity and specificity for the determination of AD in rat plasma after oral administration of AD nanoparticles. No significant interferences caused by endogenous compounds were observed. The plasma profile of AD in adult male albino wistar rats, following oral administration of the SLN formulation, was compared with the plasma profile obtained following administration of drug suspension. It was found that the plasma concentration profile of AD-SLNs represents greater improvement in drug absorption than the AD suspension.

The cetyl alcohol-derived AD-SLNs showed better pharmacokinetic profile as compared with AD-SLNs prepared by gelucire 50/13. The AUC and C\text{\textsubscript{max}} of cetyl alcohol-derived SLNs were higher than those of gelucire 50/13-derived SLNs. This may be due to smaller particle size (154.1 \pm 10.7 nm) and high entrapment efficiency (91.4 \pm 0.4 %) of AD-SLN prepared by cetyl alcohol.

The AD-SLNs prepared by cetyl alcohol were selected for antitumor activity on the basis of various pharmaceutical attributes like smaller particle size (154.1 \pm 10.7 nm), higher entrapment efficiency (91.4 \pm 0.4 %), better release profile (77.89% drug release in 36 h),
and higher AUC ($37.044 \pm 9.15 \mu g \ h \ mL^{-1}$) and $C_{\text{max}}$ ($3.272 \pm 0.7 \mu g \ mL^{-1}$), which result in better absorption thereby increasing the bioavailability of AD.

In vitro cytotoxicity study showed that AD-SLNs were as effective as free AD in arresting cell growth in all the tested cell lines (MCF-7: Human breast cancer cell line; HT-29: Human colon cancer cell line; Hep G2: Human Liver cancer cell line; SiHa: Human cervical cancer cell line; colo 320: Human colon cancer cell line; A549: Human lung cancer cell line; Hela: Human cervical cancer cell line). The results stated that AD-SLNs possessed more antitumor effect than AD, which could be attributed to an increased solubility and dissolution rate of the drug-loaded SLNs.

In vivo antitumor study revealed that the developed AD, AD-SLNs and 5-FU have a remarkable anti-tumor activity against EAC cells treated mice. In EAC-tumor bearing mice, there was a regular rapid increase in the ascetic-tumor volume, which was decreased after treatment with AD, AD-SLNs and 5-FU. The treatment groups decreased the tumor volume, tumor weight, viable tumor cells, and increased the life span of tumor-bearing mice by decreasing the nutritional fluid volume and arresting tumor growth. The AD-SLNs showed good antitumor activity, which was better than the AD and comparable to 5-FU. The AD-SLNs showed more than 80% reduction in tumor regression parameters, 5-FU showed 90% reduction, whereas AD showed only 50-60% reduction. In conclusion, the AD-loaded SLNs would potentially be useful for delivering poorly water-soluble AD with an enhanced bioavailability and improved antitumor activity.

FUTURE DIRECTIONS

- Detailed safety study of AD-SLNs
- $\gamma$-scintigraphy studies to check the bio-distribution study of AD-SLNs
- Antitumor effect of AD-SLNs on different solid tumors model
- Antitumor activity of AD-SLNs in combination with established standard drugs available for the treatment of solid tumors
- Antitumor activity of AD-SLNs in immune-compromised (nude) animals