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A simple accurate and precise method for the determination of streptomycin sulphate (STRS) was established both spectrophotometry by derivatisation (colorimetrically) and via the microbioassay method described in I.P. with suitable modifications, for application to pharmacokinetic determinations and evaluation of STRS-SLNS. The low cost of derivatising agent (SNP) in case of colorimetric determinations and the ease of performance, sensitivity and specificity for the microbiological assay are some advantages associated with the developed methods.

Presently, we explored oral and intranasal route of administration for streptomycin sulphate loaded solid lipid nanoparticles (STRS-SLNs) as an alternative to invasive parenteral (i.m) route. The former can improve patient compliance with therapy and the use of SLNs can result in achieving better or similar effect with the same or lower dose (Kaur and Singh, 2014). STRS-SLNs showed 11.0 and 7.7 times higher C\text{max} and improved BA (AUC\text{0-\infty}) with respect to F-STRS when administered by the IN route. Further to it, STRS concentration was not detectable in plasma when former was administered orally as F-STRS, while a C\text{max} of 36.08±1.8 µg/ml and AUC\text{0-\infty} of 2051.05 ±13.21 h*µg/ml was achieved when STRS was administered as SLNs. Reducing the dose or plasma concentration of free drug (most of the drug in circulation will be in the encapsulated form acting as a depot from which free drug is released slowly and over a prolonged period) is of utmost importance in case of streptomycin, considering the severe and irreversible side effects reported with its use. These side effects are directly associated with the concentration of free drug in plasma (Berkman et al., 1947). Use of STRS-SLNs may also overcome the problem of its use for a limited period of time i.e. not more than 2-3 months even though the complete anti-tubercular therapeutic regimen constitutes an atleast 9 months of therapy which may even extend to one and a half year in case of tubercular meningitis. It may be noted that a major concern with streptomycin use is the induction of resistance, which is primarily attributed to its poor cytoplasmic permeability across the mycobacterial plasma membrane (Chambers, 2005). SLNs can overcome this barrier to STRS permeability, assigning it with an
improved susceptibility of *Mycobacterium* and lowered incidence of producing resistant strains. Same was confirmed presently when the STRS-SLNs showed a log 1.5 times higher bactericidal capacity for intracellularly (in macrophages) present *S. aureus* infection in comparison to F-STRS. The MIC of developed STRS-SLNs was invariably reduced by two times when tested against a battery of standard ATCC strains and clinical isolates of *S. aureus*, again establishing the improved efficacy of STRS upon its incorporation into SLNs.

A validated, highly sensitive and specific ultra-performance liquid chromatography technique for the quantization of all-trans retinoic acid (ATRA) and vitamin D₃ with LOD of 0.5ng/ml for both the vitamins, and linearity range from 1.0 ng-5000.0 ng/ml at r²=0.999, was presently developed in rat plasma. The method was successfully applied for in vitro characterization of ATRA and vitamin D₃ loaded SLNs in terms of total drug content, entrapment efficiency, determination of stability including photostability of ATRA and vitamin D₃ loaded SLNs and their pharmacokinetic evaluation upon oral and subcutaneous administration, indicated for the treatment/prophylaxis of tuberculosis.

Both ATRA and vitamin D₃ are light and air sensitive and water insoluble molecules which are not readily absorbed from gastrointestinal tract; we incorporated these agents into SLNs comprising hydrophilic tween 80, and evaluated their pharmacokinetic profiles post administration by oral and subcutaneous routes. Intent was to achieve a controlled and sustained release of these vitamins so as to maintain their therapeutic concentrations in plasma.

Low serum level of ATRA and vitamin D₃ is observed in tuberculosis patients. In our study we could achieve and maintain more than significant plasma concentrations of ATRA in plasma for 48 h, post administration of a single oral and subcutaneous dose. The developed formulation can thus be successfully explored clinically for the treatment/prophylaxis of tuberculosis. Presently we also ascertained that incorporating vitamin D₃ into SLNs protected it against degradative effects of light and air with significantly enhanced bioavailability post administration both by the subcutaneous and oral route. Potential of vitamin D₃-SLNs is also
revealed from the maintenance of significant concentrations of vitamin D$_3$ in plasma even after 48 h post administration of single dose by either route. Vitamin D$_3$-SLNs are proposed herein as an intervention for tubercular patients, once the pharmacodynamic proof of this concept for the treatment of tuberculosis is established.

The developed oral and subcutaneous SLN formulations of both the vitamins can also be extended to treat more deadly diseases like cancers, in addition to their use for vitamin A or D related nutritional and therapeutic supplementation.