Rhein methotrexatedecorated solid lipid nanoparticles altering adjuvant arthritis progression

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\section*{Introduction}
Methotrexate (MTX) and Diacerein (DIA) are two of the most potent Disease-Modifying Anti-Rheumatic Drugs used for the treatment of Rheumatoid arthritis (RA). DIA has reflected some GIT and hepatobilary manifestations in numerous cases. It undergoes biotransformation in the liver into the active metabolite Rhein (RH) which is characterized by its excellent anti-inflammatory activity and lower side effects. However, the hydrophobic nature of RH together with its low bioavailability does not encourage its use in RA. The current study aims to use RH in combination with MTX in targeted Solid Lipid Nanoparticles (MTX-RH-SLNs) for better effectiveness and lower adverse effects.

\section*{Materials and Methods}
MTX-RH-SLNs were prepared using the high shear homogenization method and assessed for their quality attributes including particle size, zeta potential, entrapment efficiency, and structural properties using transmission electron microscopy.

The effect of the formulation was assessed in-vivo in adjuvant arthritis (AA) animal model.

\textbf{Experimental Groups:}

\begin{itemize}
  \item I. Non-arthritis healthy control rats (NC)
  \item II. AA rats -oral dose of vehicle
  \item III. AA rats -methotrexate (MTX, 1 mg/kg/week; i.p.)
  \item IV. AA rats -oral dose of Rhein solution (RH; 10 mg/kg)
  \item V. AA rats -oral dose of MTX and RH solution (MTX 150 μg/kg -RH10 mg/kg)
  \item VI. AA rats -oral dose of MTX in solid lipid nanoparticles (MTX-SLNs; 150 μ g/kg).
  \item VII. AA rats -oral dose of RH in solid lipid nanoparticles (RH-SLNs; 10 mg/kg).
  \item VIII. AA rats -oral dose of MTX and RH in solid lipid nanoparticles (MTX-RH-SLNs)
\end{itemize}

Tested drugs were administered for 15 days, from day 14 to the day of the end of the study (day 28 from adjuvant injection).

\section*{Results}

\begin{itemize}
  \item **Conclusions**
  Results revealed that MTX-RH-SLNs were in the suitable nanosize range with high negative zeta potential indicating good stability. In-vivo, MTX-RH-SLNs significantly improved all measured inflammatory and arthritic markers, confirmed by electron microscopy, immunohistochemistry, and histology examination of the joints. In conclusion, MTX-RH-SLNs can represent a promising therapeutic approach for RA.
\end{itemize}

\section*{References}