AIMS AND OBJECTIVES
The use of dietary unsaturated fatty acids in the form of conjugated anticancer drug has recently been considered as a valuable approach for the treatment of cancer. Moreover, effectiveness of such conjugated-fatty acids in cancer prevention has emerged them as promising molecules in anticancer drug designing. Fatty acid-substituted propofol analogues have received very little attention despite the fact that such molecules may emerge as potential pharmaceutical molecules. The available literature on fatty acid–substituted propofol analogues is extremely scarce. So far, no other information on their suitability as potential anticancer agents in animal models has been published. In the present effort, synthesis and characterization of four selected unsaturated fatty acids viz., ricinoleic acid, oleic acid, arachidonic acid, and linoleic acid with two different isomers of propofol has been established. Besides evaluating their \textit{in vitro} anticancer potential the study has been extended to determine their efficacy using various nanoparticle formulations in Swiss albino mice.

Along with the above mentioned work, the last chapter of the study deals with the role of siRNA in cancer therapy. siRNA entrapped in escheriosome nanoparticles were selected for treatment of liver cancer and their feasibility as anticancer agent is determined \textit{in vivo}.

\textit{Plan of Work:}

This thesis, therefore, presents and discusses the information collected on the above aspects under the heads and subheads as follows:

\begin{itemize}
\item[(1)] \textbf{Synthesis of eight novel propofol-FA analogues by conjugating:}
\begin{itemize}
\item[a)] Oleic acid with 2,4-propofol and 2,6-propofol, separately.
\item[b)] Arachidonic acid with 2,4-propofol and 2,6-propofol, separately.
\item[c)] Ricinoleic acid with 2,4-propofol and 2,6-propofol, separately.
\item[d)] Linoleic acid with 2,4-propofol and 2,6-propofol, separately.
\end{itemize}
\end{itemize}
Visualization of synthesized product on TLC slides.

(2) **Characterization of synthesized compounds employing various spectroscopic techniques:**

   a) UV absorbance spectroscopy  
   b) Fourier transform infrared (FT-IR) spectroscopy  
   c) $^1$H and $^{13}$C Nuclear Magnetic Resonance (NMR)  
   d) FAB Mass spectroscopy

(3) **Determining the extent of anticancer potential of synthesized compounds in a panel of cancer MDA-MB-361, HepG2, SK-MEL-1, A549 and non-cancer HFL1 cell lines by:**

   a) MTT assay for evaluating the cytotoxicity in various cell lines.  
   b) *In vitro* inhibitory effect on apoptotic machinery of cancer cell lines.

(4) **Efficacy of synthesized compounds bearing nanoparticle formulations on DMBA induced skin and breast cancer and DEN induced liver cancer.**  
**For this phase following parameters were covered:**

   a) Synthesis of various nanoparticles *viz.*, PC liposomes, escheriosomes, niosomes and PLGA microspheres and entrapment of selected synthesized compounds into them.

   b) Characterization of nanoparticle formulations for their $\zeta$-potential, entrapment efficiency and release kinetics. Their *in-vitro* and *in-vivo* toxicity levels by erythrocyte lysis test and hepatic and renal toxicities in Swiss albino mice will also be determined.

   c) Induction of skin and breast cancer using DMBA and liver cancer using DEN in Swiss albino mice.
d) Determining the efficacy of compound bearing nanoparticles on the basis of tumor regression, histopathology, survival and western blot analysis of apoptotic factors in skin, breast and liver cancer tissue lysates of treated mice.

(5) In vivo anticancer efficacy EC-siRNA nanoparticles on DEN induced liver cancer. For this phase following parameters were covered:

a) Preparation of escheriosome based nanoparticles and entrapment of PLK1 siRNA into it.

b) Determination of siRNA bearing escheriosome nanoparticle formulation for its $\zeta$-potential, entrapment efficiency and release kinetics.

c) Characterization of siRNA bearing escheriosome nanoparticle using transmission electron microscopy (TEM), atomic force microscopy (AFM) and nanophox particle sizer.

d) Induction of liver cancer using DEN in Swiss albino mice.

e) Treatment of liver cancer mice using siRNA bearing escheriosome nanoparticle. Determination of their targeted anticancer therapy on the basis of histopathology, survival and western blot analysis of apoptotic factors in liver cancer tissue lysates of treated mice. Determination of caspase-9 level by confocal microscopy.