Chapter II

Aims and Objectives
II.1 Aims

As discussed above in the review of literature section, plant-derived phytochemicals have enormous potential as cancer chemopreventive as well as chemotherapeutic agents and some of which are already in the market as FDA approved anticancer drugs. Furthermore, our preliminary published reports highlight important anticancer activities of decursin and acacetin against many cancer models. Therefore, present study, using decursin and acacetin and employing various in vitro as well as in vivo models, was taken up to study their:

(A) antiangiogenic activities with associated mechanisms and
(B) anticancer activities with associated mechanisms

As we observed in our preliminary studies that these phytochemicals strongly inhibit the growth and proliferation of HUVEC and various PCa cells in vitro; therefore, we tried to unravel the possible mechanisms of this inhibition and important signaling molecules involved. Since, angiogenesis plays a critical role in the malignant progression of cancers including PCa, and also that antiangiogenic targeting has been suggested as one of the most promising anticancer strategies; therefore, we tried to explore the anti-angiogenic activities of decursin and acacetin using various angiogenic models. Furthermore, in PCa their roles as anticancer as well as anti-angiogenic agents have not been evaluated so far, and we will be the first to evaluate in detail such roles using a range of in vitro as well as in vivo models. This study will identify promising molecular targets of these agents in PCa that could offer scope for further pre-clinical and clinical studies in this direction.

Therefore, keeping in view the above observations and speculations, we tied to assess the effects of these agents in HUVEC and PCa cells on mitogenic, cell survival and angiogenic signaling circuits since; these pathways are involved in cell proliferation, survival, angiogenesis and cancer progression. To prove our hypothesis, we followed a set of following specific objectives by employing the standardized methodology discussed in the following sections. Doses of decursin and acacetin selected for the present study are quite safe and nontoxic, and have already been followed in various published reports mentioned above.
II.2 Objectives

1. Chemo-modulatory effects of phytochemicals such as decursin and acacetin on *in vitro* and *ex vivo* angiogenesis
2. Effects of decursin and acacetin on *in vivo* angiogenesis
3. Mechanistic studies, including cell signaling, associated with antiangiogenic effects of these phytochemicals in Human Umbilical Vein Endothelial Cells (HUVEC)
4. Study of antiangiogenic activities of these phytochemicals in human prostate cancer cells
5. Examine anticancer activities of decursin and acacetin in human prostate cancer