3.0 OBJECTIVE OF THE WORK

Aspirin chemically acetylsalicylic acid (ASA) is in wide application for its anti-thrombolytic, antipyretic and anti-inflammatory activity by irreversible inhibition of platelet cyclo-oxygenase thus inhibiting generation of thromboxane A2 and new finding revealed the importance of ASA for its anti-carcinoma effect. ASA is the approved as an agent to prevent transient ischemic attacks and heart stroke beyond its anti-inflammatory action. The present investigation recommending the use of ASA for moderate risk in cardiovascular events. The continuous use of ASA for 5 years sown to be effective in preventing the colorectal carcinoma proved in randomized clinical trials. Doses required for preventing the effect of colorectal carcinoma relatively high (300 to 500mg), recent studies indicates the effective use ASA at low dose (75-300mg) for long term use reduce the colorectal carcinoma. These finding provide a new interest on ASA molecule which was 100 years old for this present work. But conventional aspirin suppositories usage suffers with disadvantages such as irritation, ulceration fallowed by internal bleeding.

The objective of the present work was to prepare suppositories loaded ASA-nanoparticles which will deliver therapeutic quantity of ASA nanoparticle in five steps release mechanism.
Figure 3.1. Schematic representation mechanism involved in suppositories loaded nanoparticles.

**Step 1.** Delivery of suppository into the rectal cavity.

**Step 2.** Dissolution or Melting of suppository and release of nanoparticles.

**Step 3.** Entry of nanoparticles in to the vein through fenestrated capillaries.

**Step 4.** Diffusion type of release from the nanoparticles.

**Step 5.** Nanoparticles whose size is limited for entry through fenestrated capillaries continue to release at the rectal site to their mucoadhesive properties.

In the present work ASA-nanoparticles were prepared based on ionic gelation method employing chitosan as a carrier and Sodium Tripolyphosphate (STPP) as a crosslinking agent. The effect of process variable on drug release behavior, entrapment and other characterization studies performed and best formulations isolated for incorporation. ASA-suppositories prepared using fusion method for the selection of suitable glycerogelatin base composition. Various characterization studies performed to
identify the best base composition. Finally the isolated nanoparticles were incorporated into the glycerogelatin base to prepare the suppositories loaded ASA-nanoparticles. The prepared ASA-suppositories and suppositories loaded ASA-nanoparticles were evaluated for pharmacokinetics and safety in rabbits.
3.1 PLAN OF THE WORK

The present work “Conception and evaluation of suppositories loaded nanoparticles as drug delivery system” planed to carry out in five phases.

Phase I

1. Literature review
2. Selection and collection of raw material
3. Identification of raw material
4. Preformulation studies
   - Drug polymer interaction studies by FTIR
   - Drug polymer interaction studies Differential scanning Calorimetry (DSC)
   - Development of analytical methods for (UV-VIS spectrophotometric and HPLC)

Phase II

1. Formulation and evaluation of ASA-nanoparticles (formulation variable 1. chitosan concentration 2. STPP)
2. Formulation and evaluation of ASA-suppositories.
3. Formulation and evaluation of suppositories loaded ASA-nanoparticles.

Phase III

1. Formulation and evaluation and in-vitro release study of ASA-nanoparticles and effect of process variables (Chitosan, STPP).
2. Formulation and evaluation of ASA suppositories and suppositories loaded ASA nanoparticles.
3. *In-vivo* safety and pharmacokinetic study of ASA-suppositories and suppositories loaded ASA nanoparticles.


**Phase IV**

1. Summary
2. Results and discussion
3. Conclusion
4. Recommendations
CONCEPTION AND EVALUATION OF SUPPOSITOIRES LOADED
NANOPARTICLES AS A DRUG DELIVERY SYSTEM

Figure 3.1.1 Steps involved in preparation of suppositories loaded
ASA-nanoparticulates