2. REVIEW OF LITERATURE

Simultaneous determination of tolperisone hydrochloride and paracetamol in combined tablet dosage form by validated HPTLC method.

Comprehensive literature survey revealed that there are some analytical methods reported for tolperisone hydrochloride (TOLP) like spectrophotometric [41-44], HPTLC [45, 46] and HPLC [47-50] either individually or in combination with other drugs. Spectrophotometric [51-54], HPTLC (densitometric) [55-57], and HPLC [58-66] methods of analysis have been reported for paracetamol (PCM) individually or in combination with other drugs.

Densitometric (HPTLC) method for concurrent estimation of rosuvastatin calcium and fenofibrate in bulk and tablet (pharmaceutical) dosage form.

The thorough literature survey showed that few analytical methods are available for rosuvastatin calcium (ROS) and fenofibrate (FEN). UV spectrophotometric methods [67-69], high performance thin layer chromatography methods [70-72] and high performance liquid chromatographic methods [73-76] for ROS and FEN was analyzed in bulk and in formulations using methods like UV analysis [77-80], densitometric methods [81, 82] and HPLC analysis [83-87].

Tandem mass (LC-MS/MS) method development and validation for the concurrent analysis of paracetamol, guaifenesin, phenylephrine hydrochloride, chlorpheniramine maleate, and ambroxol hydrochloride in bulk and combined tablet formulation.

A detailed literature survey revealed spectrophotometric [88, 89], HPTLC [90, 91], and HPLC [92-96] analytical methods have been reported for guaifenesin (GUA) individually or in combination with other drugs. Literature survey reflected spectrophotometric [97, 98], HPTLC [99-102], and HPLC [103] methods of analysis for ambroxol hydrochloride (AMB) individually/in combination with other drugs. Spectrophotometric [104, 105], HPTLC (densitometric) [106, 107], and HPLC [108-112] analytical methods have been reported for chlorpheniramine maleate (CPM) individually or in combination with other drugs. Literature survey showed that
spectrophotometric [113, 114], HPTLC [115], and HPLC [116-119] techniques have been reported for phenylephrine hydrochloride (PE) individually or in combination with other drugs.

Detail literature survey reveals that individual analytical methods are available for selected drugs, but no HPTLC and LC-MS/MS method is available for their concurrent analysis. Hence, in the present research attempt will be made to develop, validate chromatographic (HPTLC/hyphenated technique) methods for pharmaceutical formulations using active pharmaceutical ingredients/standards. Therefore aims, objectives of the present research work are as follows,

- To develop HPTLC method for Concurrent determination of paracetamol and tolperisone hydrochloride in bulk drug as well as in the combined (pharmaceutical) dosage form.
- To develop densitometric (HPTLC) method for simultaneous determination of rosuvastatin calcium and fenofibrate in bulk drug and in combined pharmaceutical formulation.
- To develop LC-MS/MS method of analysis for simultaneous estimation of paracetamol, guaifenesin, phenylephrine hydrochloride, chlorpheniramine maleate, and ambroxol hydrochloride in bulk drugs as well as in combined tablet dosage form.
- To validate the proposed HPTLC and LC-MS/MS methods as per ICH [Q2 (R1)] guideline.

To achieve the set aims, objectives of the work, the research is designed as follows,

1. **Selection of drug/drug combinations.**
   Extensive literature and the market survey will be carried out for selection of suitable drug/drug combinations and their combined formulations.

2. **Analytical methods selection.**
   For the simultaneous estimation of selected drug/drug combinations and their combined formulations chromatographic methods like HPTLC and Tandem mass spectrometry (LC-MS-MS) will be selected, on the basis of literature survey.
3. Development and validation of a densitometric method for concurrent analysis of tolperisone hydrochloride and paracetamol in bulk drugs and in the pharmaceutical dosage form.

- **Study of Solubility behavior of drugs**
  The solubility of selected drug combinations will be checked in different organic solvents having a wide range of polarity indices.

- **Selection of maximum absorption wavelength**
  The $\lambda_{\text{max}}$ will be determined from UV-Visible spectrum obtained by UV spectrophotometer/HPTLC instrument.

- **Method development**
  Optimization of the method will be carried out through well designed experiments and statistical analysis of data.

- **Validation of the method and statistical evaluation**
  Validation of the analytical method in accordance with ICH Q2 (R1) guideline and statistical evaluation will be performing.

- **Marketed formulation analysis**
  The proposed validated method will be applied for estimation of drugs in the combined pharmaceutical dosage form.

4. HPTLC method development and validation for densitometric analysis of rosuvastatin calcium and fenofibrate in bulk drugs and their combined formulation.

- **Solubility and stability studies**
  Solubility of selected drugs will be checked in different wide range polarity organic solvents.

- **$\lambda_{\text{max}}$ Selection**
  The $\lambda_{\text{max}}$ will be determined from UV-Visible spectrum obtained by UV spectrophotometer/HPTLC instrument.

- **Method development**
  Optimization of the analytical method will be carried out through well designed experiments and statistical analysis of data.

- **Validation of the method and statistical evaluation**
  Validation as per ICH Q2 (R1) guideline of the developed method and statistical evaluation will be carried out.
- **Marketed formulation analysis**
  Planned validated method will be applied for quantification of drugs in the combined pharmaceutical formulation.

5. **LC-MS/MS method of analysis for simultaneous estimation of paracetamol, guaifenesin, phenylephrine hydrochloride, chlorpheniramine maleate and ambroxol hydrochloride bulk drugs as well as in combined dosage form.**

- **Solubility and stability studies**
  Solubility of selected drugs will be checked in different organic solvents.

- **Development of analytical method**
  Optimization of the analytical method will be carried out through well designed experiments and statistical analysis of data.

- **Optimization of LC conditions**

- **Validation of the method and statistical evaluation**
  Validation of the developed LC/MS/MS method by using different statistical parameters.

- **Analysis of marketed formulation**
  Proposed validated method will be applied for estimation of drugs in the combined marketed formulation.