FORMULATION AND EVALUATION OF DICLOFENAC SODIUM INJECTION

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Abstract

This study focuses on the formulation and evaluation of a stable injectable dosage form of diclofenac sodium, a non-steroidal anti-inflammatory drug (NSAID) with exceptional analgesic properties. The aim was to develop an effective parenteral solution suitable for intramuscular and intravenous administration, addressing the challenges posed by diclofenac sodium's low solubility and ensuring patient comfort during administration. The injectable formulation was prepared using solubilizing agents and excipients, and evaluated for key parameters including solubility, pH, osmolarity, physical appearance, weight per mL, and assay by HPLC. Results confirmed that the formulation met pharmacopoeial standards, with a clear, colourless appearance, a pH of 8.5, osmolarity of 568 mosm/kg, and 98.6% drug content. The findings indicate that the developed diclofenac sodium injection is stable, effective, and clinically suitable for treating a variety of acute and chronic pain conditions, ensuring reliable drug delivery and patient safety.

Introduction

Diclofenac is a commonly used medication for treating a variety of pain conditions, including both acute and chronic painful episodes, because of its exceptional analgesic qualities. The medication is used to treat soft tissue disorders like sprains and strains, periarticular disorders like bursitis and tendonitis, musculoskeletal and joint disorders like rheumatoid arthritis, acute gout, and dysmenorrhea, as well as painful conditions like renal colic, acute gout, dysmenorrhea, and post-surgery (1). In particular, the treatment must be effective against the pain, photophobia, phonophobia and nausea that are caused by migraine and it must be effective within the first 2 h of treatment, to be considered a true treatment for migraine. The aim of the current study aims to develop, formulate and evaluate diclofenac sodium injection (2). Diclofenac sodium is a non-steroidal anti-inflammatory drug (NSAID) with the chemical structure ((2,6-dichloroanilino)-2-phenyl)-2-acetic acid and is classified as a Biopharmaceutics Classification System (BCS) class II drug, indicating low solubility and high permeability. This study focuses on stable parenteral aqueous solutions of diclofenac sodium for intramuscular or intravenous administration (3).

Drug profile

Diclofenac Sodium

- Name: Diclofenac Sodium
- Classification: Non-Steroidal Anti-Inflammatory Drug (NSAID)
- Chemical Name: ((2,6-dichloroanilino)-2-phenyl)-2-acetic acid
- Molecular Formula: C14H11Cl2NO2
- Molecular Weight: 318.13 g/mol
- Biopharmaceutics Classification System (BCS): Class II (low solubility, high permeability)

Pharmacokinetics

- Absorption: Rapidly absorbed following oral or parenteral administration; bioavailability is affected by first-pass metabolism.
- Distribution: Highly protein-bound (99%) to albumin.
- Metabolism: Extensively metabolized in the liver via CYP2C9 to hydroxylated and conjugated metabolites.
- Elimination Half-Life: 1–2 hours.
- Excretion: Primarily excreted in urine (~65%) and feces (~35%).

Mechanism of Action

Diclofenac inhibits cyclooxygenase (COX-1 and COX-2) enzymes, reducing the synthesis of prostaglandins, which are mediators of pain, inflammation, and fever.

Storage:

Keep in a cool, dry place; injectable solutions should be stored as recommended to maintain stability.

Aim & objective

Aim

To develop, formulate, and evaluate a stable injectable dosage form of diclofenac sodium for intramuscular and intravenous administration.

Objectives

- To formulate an injectable solution of diclofenac sodium using suitable solubilizing agents and excipients.
- To ensure the formulation provides effective drug delivery without causing pain at the administration site.

Materials and Methods

Materials

Diclofenac sodium and other reagent & excipients was procured as a gift sample from Freedom biopharma, Hosur. Other materials and Instruments include digital weighing balance(Redwag),digital ph meter(Eutech), Hot air oven(Allyone), Sonicator(Roop Telsnic Ultrasonix Ltd), Osmometer(Advanced instrument), Humidity chamber(Asha scientifiv company, Mumbai), HPLC(Shimadzu L (92050c HPLC)).

Method

The area was cleared of any previous products and materials. Fifty liters of Water for Injections (WFI) were collected in a sterile vessel and purged with nitrogen for 10 minutes. A sample was then sent to Quality Control (QC) for analysis. Upon QC approval, the WFI was used for manufacturing.

Twenty liters of cool WFI were taken, and 1.5 kg of Mannitol was dissolved under constant stirring until fully dissolved. The solution was sparged with 0.2 µm filtered nitrogen. Subsequently, 1.04 liters of Benzyl Alcohol and 5 kg of Propylene Glycol were mixed

thoroughly in a 12.5-liter stainless steel vessel. This mixture was stirred continuously and added to the solution under constant agitation.

Seventy-five grams of Sodium Metabisulfite were dissolved in the mixture, followed by agitation until fully dissolved. The solution was again sparged with 0.2 µm filtered nitrogen. The calculated quantity of Diclofenac Sodium was added, and the mixture was agitated until the drug was completely dissolved. Nitrogen sparging was continued during this process.
The pH was checked and recorded. The final volume was made up to 25 liters using WFI, and the solution was stirred for 15 minutes with continuous nitrogen purging. The final pH (within the limit of 8.1 to 9.0) was checked and recorded, and a sample was sent to QC for bulk analysis.

Evaluation of formulation injection

Physical appearance

Transferred about 10ml of the sample into a colourless test tube having a inside diameter of 15-25mm and observed against a white background for color and black background for clarity.

pH measurement

Taken approximate 50 ml of sample solution in 50 ml beaker and checked the PH of the solution used calibrated PH meter.

Osmolarity:

The osmolarity of prepared formulations and the marketed product was determined used a freezing-point based osmometer advance instruments was used for the study.

Weight per mL:

Cleaned and dried the pycnometer and weighed (W1). Fill the pycnometer with water at 20°C up to the mark and weighed (W2). Cool the test solution to about 15°C. Rinsed the pycnometer with test solution filled the pycnometer with test solution up to the mark. Adjusted the temperature of filled pycnometer to 20°C by dipping in water at 20°C contained in a beaker. Adjusted the sample up to the mark and weigh (W3).

Calculation:

Calculate the wt/ml as per the formula below:

$$\text{Weight per mL} = \frac{(W3-W1) \times 0.997043}{(W2-W1)}$$

Water density 0.997043 as per USP.

Assay by HPLC:

Table 1: List of the chemicals

Chemicals	Grade
Orthophosphoric acid	AR Grade
Sodium dihydrogen orthophosphate	AR Grade
Methanol	AR Grade

Preparation of 0.1 per cent w/v solution of orthophosphoric acid:

Diluted 0.1ml of orthophosphoric acid dissolved in 100ml of water.

Preparation of 0.16 per cent w/v solution of sodium dihydrogen orthophosphate:

Weighed accurately 0.16g of sodium dihydrogen orthophosphate dissolved in 100ml of water.

Mobile phase:

A mixture of 34 volumes of a mixture of equal volumes of a 0.1 per cent w/v solution of orthophosphoric acid and a 0.16 per cent w/v solution of sodium dihydrogen orthophosphate, adjusted to pH 2.5, and 66 volumes of methanol.

Test solution:

Diluted a suitable volume of the injection containing 50 mg of Diclofenac Sodium to 100 ml with the mobile phase. Diluted 1 ml of this solution to 10 ml with the mobile phase.

Table 2: List of Chromatographic system

Mode	LC
Column	A stainless steel column 25 cm x 4.6 mm, packed with octylsilane bonded to porous silica (5 µm),
Flow rate	1.0 ml/ min
Detector	UV Visible
Wavelength	254-nm
Injection Volume	10 µl

Calculation:

Calculated the content of $C_{14}H_{10}Cl_2NNaO_2$ in the injection.

$$\frac{\text{Area of sample}}{\text{Area of Standard}} \times \frac{\text{Wt. Std}}{50} \times \frac{5}{20} \times \frac{100}{\text{Wt.spl}} \times \frac{25}{5} \times \frac{P}{100} \times \frac{169.18}{205.64} \times \frac{X}{\text{Wt/mL}}$$

Where, P- Purity

$$\%\ \text{Assay} = \frac{\text{mg/ml} \times 100}{\text{LC}}$$

Results and discussion

Table 3: Result by Solubility of diclofenac sodium

Formulation	Solubility
Diclofenac Sodium	Freely soluble in water and sparingly soluble in alcohol

Table 4: Result by Melting point of diclofenac sodium

Formulation	Melting point (°C)
Diclofenac Sodium	284.63

Table 5: Result by Appearance of diclofenac sodium injection

Formulation	Appearance
Diclofenac Sodium injection	A clear colorless solution free from visible particles

Table 6: Result by pH measurement of diclofenac sodium injection

Formulation	PH
Diclofenac Sodium injection	8.5

Table 7: Result by Osmolarity of diclofenac sodium injection

Formulation	Osmolarity (mosm/kg)
Diclofenac Sodium injection	568

Table 8: Result by Weight per mL of diclofenac sodium injection

Formulation	Weight per mL
Diclofenac Sodium injection	1.052gm/Ml

Table 9: Result by Assay by HPLC

Formulation	Assay by HPLC
Diclofenac Sodium injection	98.6%

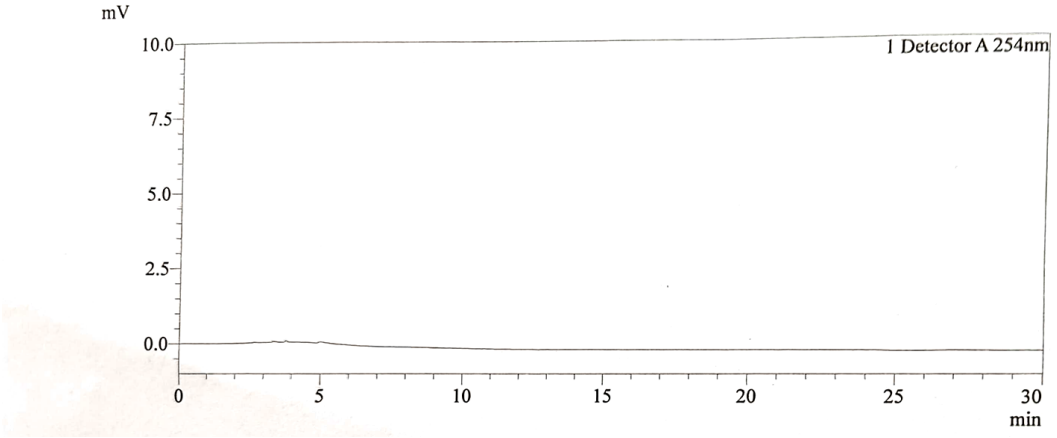

Fig 1: Chromatogram of Blank

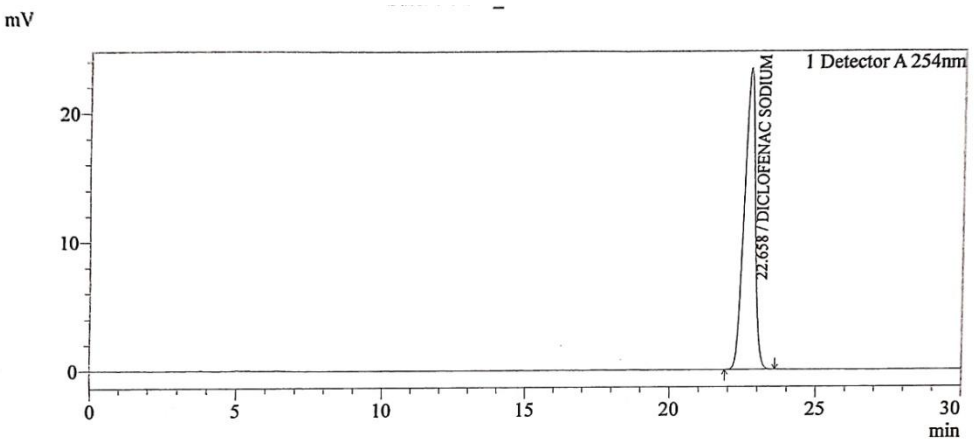

Fig 4: Chromatogram of sample preparation

Detector A 254nm

Peak#	Name	Ret Time	Area	Height
1	Diclofenac sodium injection	22.658	606611	23484
Total		607232	606611	23484

Discussion

The results of the formulation and evaluation of diclofenac sodium injection were satisfactory, meeting the established parameters. The solubility analysis confirmed that diclofenac sodium is freely soluble in water and sparingly soluble in alcohol, consistent with its classification as a BCS Class II drug. The melting point determination (284.63°C) aligns with standard values, confirming the purity of the compound.The formulated injection exhibited a clear, colorless appearance free from visible particles, indicating good physical stability. The measured pH of 8.5 falls within the acceptable range (8.1–9.0), ensuring compatibility and stability for parenteral administration. The osmolarity (568 mosm/kg) is within the physiological range, minimizing the risk of irritation or pain at the injection site.

The weight per milliliter (1.052 g/mL) confirms uniformity, and the HPLC assay indicated 98.6% drug content, reflecting high formulation accuracy and consistency. Collectively, these findings suggest that the developed injection meets pharmacopoeial standards for injectable products and is suitable for clinical application.

Conclusion

The study successfully developed and evaluated a stable parenteral formulation of diclofenac sodium injection. Key characterization parameters such as solubility, melting point, appearance, pH, osmolarity, weight per milliliter, and drug content were within acceptable limits, ensuring the formulation's quality and efficacy. This injectable formulation provides a reliable and effective delivery system for diclofenac sodium, addressing the challenges of low solubility and ensuring patient safety and comfort during administration.

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