

## Physical Stability of Rofecoxib Oral Suspension Formulated By Controlled Flocculation

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### ABSTRACT

The present work was aimed to formulate physically stable Rofecoxib suspension using controlled flocculation. Rofecoxib a selective COX-2 inhibitor is indicated in the treatment of osteoarthritis and management of acute pain and treatment of primary dysmenorrhoea and is superior to other NSAIDS due to lower incidence of bleeding and other gastro toxic effects.

The ability of different flocculating agents to flocculate Rofecoxib suspension was studied. It was also proposed to assess the physical stability of the prepared formulation by performing stability studies according to ICH guidelines. UV- spectrophotometric method was selected for assay as well as *in-vitro* dissolution studies at 237nm.

**Keywords:** Rofecoxib, physical stability, flocculated oral suspensions, NSAID.

### OBJECTIVES

Rofecoxib oral suspensions were formulated with an objective of improving the physical stability by controlled flocculation approach.

### INTRODUCTION

Rofecoxib pronounced as "ro-fa-cox-ib" chemically is 4-[4-(methyl sulfonyl phenyl)] 3-phenyl-2(5H) furonone. Which is a selective cyclooxygenase-2(COX-2) inhibitor and it is indicated for treatment of osteoarthritis and shows lower incidences of gastric bleeding and other gastro-toxic effects than the non-selective NSAIDS. Rofecoxib is a NSAID that exhibits its anti-inflammatory, analgesics and antipyretic activities in animal model. The mechanism of action of Rofecoxib is believed to be due to inhibition of prostaglandin

synthesis via selectively inhibition of COX-2. At therapeutic serum levels, Rofecoxib acid does not inhibit the cyclooxygenase-1(COX-1) Iso enzyme.

It is white to off white to light yellow powder. Sparingly soluble in acetone. Slightly soluble in ethanol and insoluble in water. Rofecoxib is used as drug in present study because it is insoluble in water, it is a suitable drug for preparing suspension. The present work as aimed to formulating physically stable Rofecoxib suspension controlled flocculation approach the ability of different flocculating agent to flocculate Rofecoxib suspension was studied and proposed to assess physical stability of that prepared formulations according to ICH guide lines.

**Table: showing Preparation of Rofecoxib flocculated oral suspensions**

Formulae	F <sub>1</sub>	F <sub>2</sub>	F <sub>3</sub>	F <sub>4</sub>	F <sub>5</sub>	F <sub>6</sub>	F <sub>7</sub>	F <sub>8</sub>	F <sub>9</sub>	F <sub>10</sub>
Rofecoxib	1gm	1 gm								
Methylparaben sodium	0.15%	0.15%	0.15%	0.15%	0.15%	0.15%	0.15%	0.15%	0.15%	0.15%
Propylparaben sodium	0.05%	0.05%	0.05%	0.05%	0.05%	0.05%	0.05%	0.05%	0.05%	0.05%
Sorbitol solution	10%	10%	10%	10%	10%	10%	10%	10%	10%	10%
Distilled water	100ml	-	-	-	-	-	-	-	-	-
CaCl <sub>2</sub> (10%)	-	100ml	-	5.33ml	-	6.66ml	-	0.666ml	3.33ml	-
Sodium alginate	-	-	-	-	100ml	100ml	-	-	3.33ml	-
Veegum (0.4%)	-	-	-	-	-	-	100ml	100ml	-	-
Xanthan gum (0.1%)	-	-	-	-	-	-	-	-	100ml	100ml
AlCl <sub>2</sub> (0.5%)	-	-	-	-	-	-	-	-	-	1.6ml

## PREPARATION

Suspensions containing 50mg of Rofecoxib in 5ml. were prepared as per the formula given in table. In about 100ml of pure water, the required amount of surfactant/polymer/clay was added and kept overnight for proper hydration. These respective solutions were used as the vehicle the required quantity of sorbitol was added and kept aside for 4 hrs for proper wetting. The slurry concentrate of the drug was mixed gently for 15 min. calculated amount of 10% solution of calcium chloride was added gradually to the uniformly distributed drug to achieve an optimum flocculation. Other ingredients like methyl paraben sodium were added and finally the volume was made up with the vehicle. Respective control suspension were prepared similarly omitting the electrolyte. Purified water without any flocculating agent was used as the vehicle in the preparation of suspension F<sub>1</sub>.

## EVALUATION AND STABILITY STUDIES OF SUSPENSION

There are many dimensions of a suspension dosage form that are indicative of its quality, stability acceptance and performance. The effect of natural aging on the stability of the prepared suspensions was studied. The formulative suspensions were evaluated at different time intervals for the following parameters.

- 1) Sedimentation volume
- 2) Degree of flocculation
- 3) Zeta potential
- 4) Redispersibility
- 5) Particle size measurement
- 6) pH measurement
- 7) Viscosity measurement
- 8) Drug content estimation
- 9) Dissolution studies

## CONCLUSION

From the stability studies, it was found that the suspension containing veegum, calcium chloride (F<sub>8</sub>) was the best formulation among all the suspensions prepared.

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