

Stability omeprazole 2 mg/ml suspension for use in paediatrics in different acidic media

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1. Introduction

Compounding formulas are used in hospital settings to be able to cover the needs of special patients, such as paediatric, geriatric, or other patients with inability to swallow [1]. According to data provided by the Vall d'Hebron Maternity and Children's Hospital, omeprazole is one of the most active principles used in compounding formulas, for the treatment of gastrointestinal disorders in paediatric patients. The Omeprazole 2 mg/mL formulation in xanthan gum suspension (Table 1) is frequently used in hospital pharmacy services. Omeprazole is one of the Proton Pump Inhibitors (PPIs); the most widely used antisecretory drugs due to its efficacy and lack of significant adverse effects. Its stability depends on the pH: the degradation is fast in acidic medium but remains practically stable under alkaline conditions. For this reason, it is administered orally, in capsules containing enteric-coated granules, to prevent its ionization by the gastric acidic environment and promote its absorption in the duodenum [2].

Omeprazole 2 mg/mL Suspension	
Omeprazol base	0,2 %
Sodium bicarbonate	8,4 %
Xanthan gum 1 % aqueous solution	50 mL
Vanilla essence	0,1-0,2 %
Sodium saccharin	0,1-0,3 %
Purified water q.s.	100 mL

Table 1. Omeprazole 2 mg/mL Suspension in xanthan gum.

2. Objectives

In the scientific literature, there is a lack of stability studies for the compounding formulation of Omeprazole 2 mg / mL in xanthan gum suspension. Thus, in this study it is proposed to determine the behaviour of this suspension in different pH media (1.2; 2.2 and 4.5), simulating, in this way, the variations in stomach pH.

3. Methodology

The Omeprazole 2 mg/mL formulation in xanthan gum suspension is prepared, according to the preparation protocol provided by the pharmacy service of the Vall d'Hebron Maternity and Children's Hospital [3]. And in parallel, 3 pH media (1.2; 2.2 and 4.5) are elaborate. After that, 10 mL of the suspension, an amount equivalent to 20 mg of omeprazole, are added to each of the pH media. Finally, its behaviour is observed for 2 hours.

A placebo is also prepared to verify that the change in colour of the pH media is not the result of the degradation of any excipient. Three pH 1.2 media are prepared: in the first one, 10 mL of the placebo is added, in the second, 20 mg of omeprazole pellets and in the third, 20 mg of omeprazol base. These media are also observed for 2 hours. Thus, it is intended to show that the colour changes observed in the pH media are due to the degradation of omeprazole in acidic pH [4].

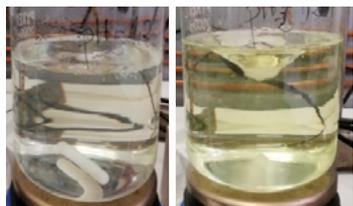


Figure 1. pH 1.2 medium. Left image: Omeprazole 2 mg/mL suspension in xanthan gum, time 0 minutes. Right image: Omeprazole 2 mg / mL suspension in xanthan gum, time 5 minutes.

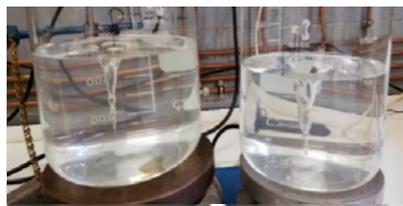


Figure 2. Left image: pH 2.2 medium; Omeprazole 2 mg / mL suspension in xanthan gum, time 5 minutes. Right image: pH 4.5 medium; Omeprazole 2 mg/mL suspension in xanthan gum, time 5 minutes.



Figure 3. The 3 pH media after 1 h and 15 min: Left: pH 1.2 medium; Middle: 2.2 pH medium and Right: 4.5 pH medium.



Figure 4. The 3 pH media after 2 h: Left: pH 1.2 medium (yellow colour); Middle: pH 2.2 medium (light brown colour) and Right: pH 4.5 medium (pink colour).



Figure 5. pH 1.2 medium with Omeprazole Base. The image on the left is after 10 minutes of adding 20 mg of Omeprazole Base. The image on the right is after 2 h of adding 20 mg of Omeprazole Base.

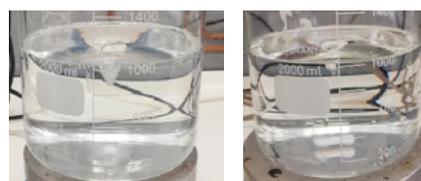


Figure 6. pH 1.2 medium with placebo. Not colour change is observed after 2 h.



Figure 7. pH 1.2 medium with enteric coated omeprazole pellets. Not colour change is observed after 2 h.

4. Results and Discussion

Omeprazole degrades rapidly in an acidic medium, for this reason when the 10 ml of the suspension are added in pH 1.2 medium, in less than 1 minute a colour change is observed, from transparent to slightly yellow. This coloration intensifies after 5 minutes, as shown in Figure 1. Respect to pH 2.2 and 4.5 media (Figure 2) after 5 minutes, they are not completely transparent, and a slight change begins to be observed. Figures 3 and 4 show how the colour changes produced in each of the pH media intensify with time. The different colours, which are observed in pH media, are probably because of the degradation of omeprazole in different metabolites, depending on the pH. Figures 5 and 6 suggest that colour change

in the pH 1.2 medium is due to the degradation of omeprazole and not to formulation excipients.

The results obtained suggest that the administration of Omeprazole 2 mg/mL formulation in xanthan gum suspension will not be effective, because omeprazole is degraded in the stomach acidic environment.

5. Conclusion

The results obtained show the instability of the suspension of Omeprazole 2 mg/mL in acidic medium. Colour changes of different acidic pH media show the omeprazole degradation. Therefore, the therapeutic efficacy of this formulation is compromised.

References

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