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Study of the Effect of pH on the Cleaning of Fexofenadine in a Stainless-Steel Reactor by the Rinsing and Swabbing Method

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Abstract: ***The cleaning in the pharmaceutical industry is involved in each process of manufacture of drugs, it assure the quality of the final product. Cleaning is a key position in the fight against the risks of cross-contamination (chemical, microbiological and particulate) of drugs. The aim of this work is the study of the influence of pH on the cleaning of fexofenadine in a stainless steel reactor. Two cleaning methods were studied, the rinsing method and the swabbing method.***

Keywords: pharmaceutical industry, fexofenadine, cleaning rinsing, swabbing, pH.

1. Introduction

The pharmaceutical industry uses in each of the manufacturing processes the dispersion of fine powders in a liquid medium.

The wettability property of a gas/liquid/solid system that results in a wetting angle β is the macroscopic consequence of molecular interactions between solid, liquid and gas [1].

This wettability property is therefore intrinsically linked to the surface molecular state of materials.

The quality required for pharmaceutical products continues to grow as scientific knowledge evolves to ensure the quality of production and to ensure the absence of cross-contamination risk. Fexofenadine is a drug in the family of antihistamines.

It presents a danger to human and animal health and a risk of flammability [2].

The purpose of this work is to study the effect of pH on the cleaning of fexofenadine in a stainless steel reactor by two methods the rinsing method and the swabbing method.

2. Material and methods

Fexofenadine is a drug from the family of antihistamines, with the formula $C_{32}H_{39}NO_4$.

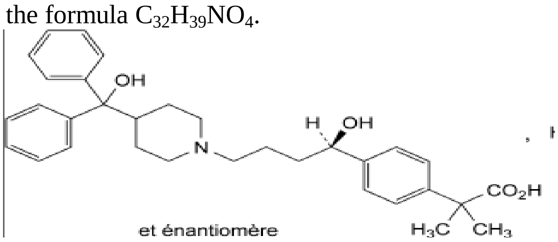

Figure 1: Chemical formula of fexofenadine

The fexofenadine nomenclature according to IUPAC is:

2- [4 - [(1-Hydroxy-4- [4- (hydroxyl diphenyl methyl) piperidin-1-yl] butyl] phenyl] -2-dimethylpropanoic acid, having a molar mass of 501.6564 ± 0.0297g / mol, its melting temperature is about 142.5 ° C.

Fexofenadine is a white or substantially white powder [3].

For each sampling method five pH's are studied; pH equal to 4; 3.5; 3; 2.5 and 2.

The pH is adjusted using a solution of 1M (HCl).

The pH is measured using a CRISON® BASIC pH-meter pH meter.

To analyze the solutions and determine their concentrations, a branded spectrophotometer (Optizen POP) with a 1cm optical path (quartz vats) was used for a 276 nm wave housewave.

The cleaning validation of fexofenadine is followed by both sampling methods the rinsing and the swabbing.

2.1 Rinsing method

This method involves contaminating the reactor with a known amount of the drug. Then, three consecutive rinses are performed by filling the reactor with water each time. Absorbance at each rinse is measured by performing 3 readings on each diluted 3 times.

Distilled water is used as white.

To study the cleaning of fexofenadine by the rinsing method, a cylindrical reactor of 18.8 cm internal diameter, 19.4 cm external diameter, 14.5 cm high, 850.65 cm² internal surface and 4L, is used volume (Figure. 2).

Figure 2: Reactor used [4].

2.2. Swabbing method

Water is chosen as a cleaning solvent.

A stainless steel plate is used to study the cleaning of fexofenadine. A square area of 10x10cm ($100cm^2$) is contaminated with 5mL of fexofenadine solution.

Cotton swabs 15cm in length are used.

Five swabs are immersed in a beaker containing the extraction solvent and then pressed against the wall of the beaker to wring them out.

The surface is swabbed for 60 seconds, wiping upward on one side and left to right on the other side of the swab, this swab is introduced into a 25 mL beaker containing 10 mL of water. Swabbing should be done over the entire surface of the swab, applying gentle pressure at the time of sampling. This operation is repeated using 3 other wet swabs on the same surface and then introducing them into the same beaker as the first swab. Using a dry swab, the surface is swabbed for 60 seconds and the swab is introduced into the same beaker as the others.

The swabs are removed from the beaker after being squeezed against the walls, swabbing all the swabs at the same time against the walls of the beaker, and then rotating the swab stems by rubbing between the palms of the hands.

The solution is analyzed by visible UV.

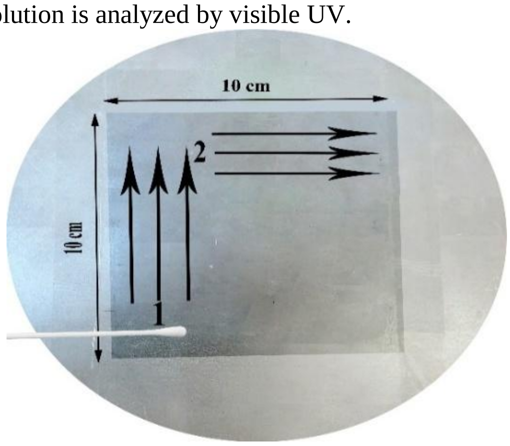

Figure 3: Method of swabbing a stainless steel surface.
Space/Gap between Columns - 5.0 mm (0.2").

3. Results and Discussion

The calibration lines corresponding to the absorbance versus concentration used to calculate the fexofenadine concentration are shown in Fig. 4.

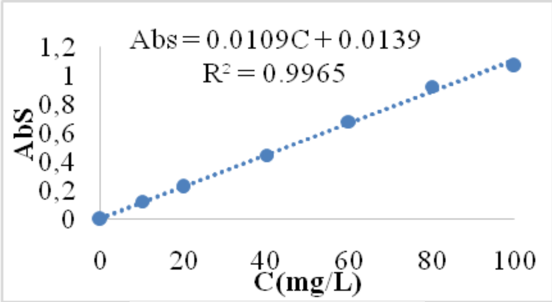

Figure 4: Calibration lines.

The study is conducted by studying pH equal to 4; 3.5; 3; 2.5 and 2 for both sampling methods (rinsing and swabbing).

For pH equal to 2.5 and 2; the absorption spectra (Figures 5 and 6) show that the fexofenadine molecules hydrolyze.

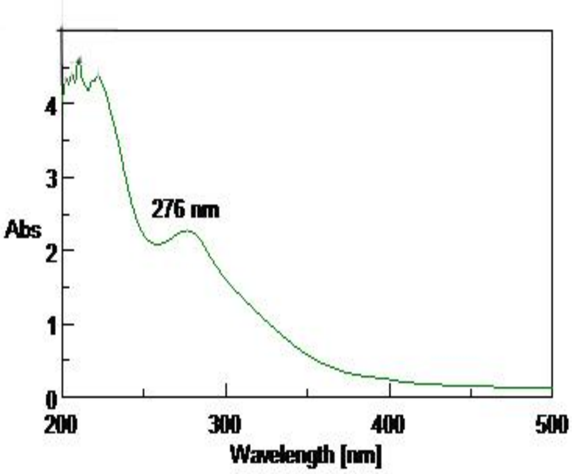

Figure 5: Absorption spectrum of a cleaning solution at pH = 2.5

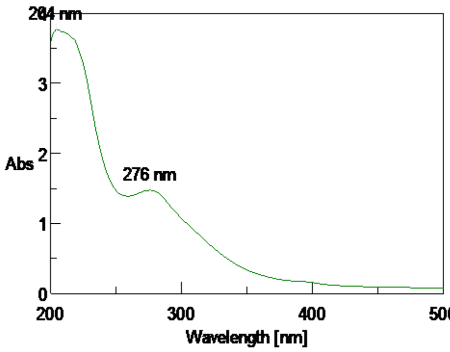

Figure 6: Absorption spectrum of a cleaning solution at pH = 2

3.3.1 Rinsing method

The results of the residual concentration (CR) during the cleaning for the five pHs studied are shown in figure 7.

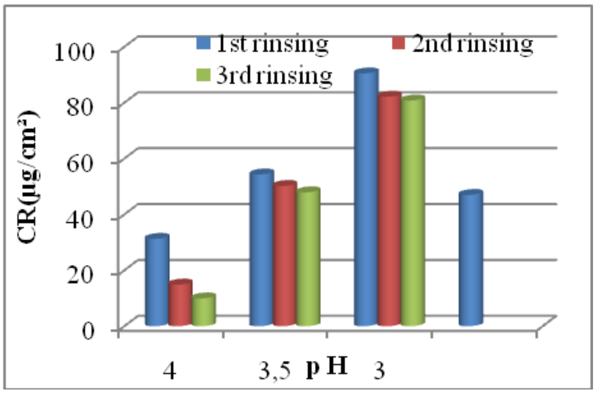

Figure 7: Variation of the residual concentration of the three rinsings as a function of the pHs studied.

For the pH equal to 4 (free pH); the residual concentration decreases from 31.30 to 9.99 µg / cm² during the three rinses.

For the pH equal to 3.5; the residual concentration decreases from 54.33 to 47.497 µg / cm² during the three rinses.

For the pH equal to 3; the residual concentration decreases from 90.51 to 80.78 µg / cm² during the three rinses.

The residual concentrations for the pH equal to 4 are below the acceptance threshold (47.022 mg / cm²) so cleaning is satisfactory from the 1st rinse. The performance results of the concentration rinsed during the cleaning for the four pHs studied are shown in fig. 8.

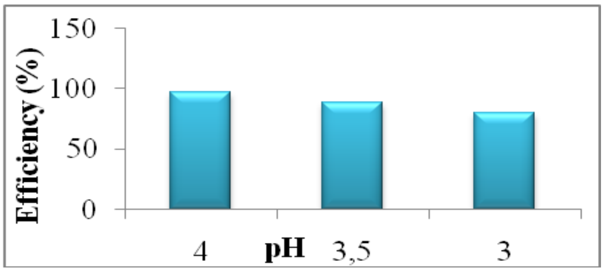

Figure 8: Efficiency of the rinsed concentration after the three rinsings as a function of the pHs studied. For the pH equal to 4 (free pH), the yield of the rinsed concentration is 97.57%

For the pH equal to 3.5: the yield of the rinsed concentration is 88.36%.

For the pH equal to 3: the yield of the rinsed concentration is 80.36%.

3.2 Swabbing method

The results of the residual concentration (CR) during the cleaning for the three pHs studied are shown in fig. 9.

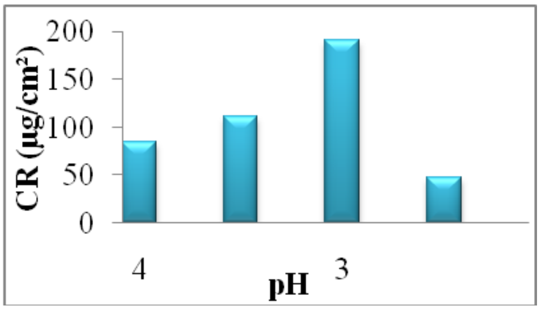

Figure 9: Change in residual concentration as a function of pH during swabbing.

These results show that the residual concentration of fexofenadine increases with decreasing pH.

The results of the concentration yield rinsed during the cleaning for the three pHs studied are shown in fig. 10.

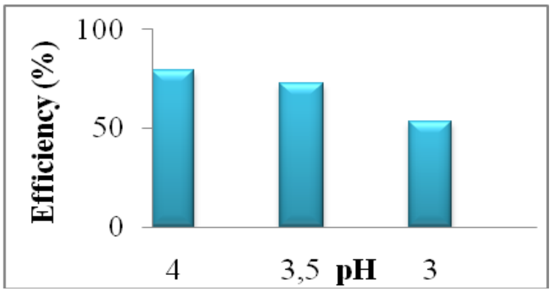

Figure 10: Efficiency of rinsed concentration after swabbing as a function of pH.

For pH equal to 4, the yield of the rinsed concentration is 79.53%. For pH equal to 3.5, the yield of the rinsed concentration is 72.77%.

For pH equal to 3, the yield of the rinsed concentration is 53.51%.

pH plays an important role in the solubility of chemical molecules, especially dissolved gases in aqueous media. This will have an effect on the wetting state and therefore on the interfaces (solid, liquid, gas).

Nevertheless, it has been shown that a hydrophilic character of the material does not always generate superhydrophilic states for the textured surface both for open surfaces of nano-pillar network types [5] and surfaces with closed structures of nanotrous type [6] or porous materials whose porosity is nanometric [7].

For all of these cases, partial wetting conditions are observed because the air remains trapped inside the texturing.

The kinetics of dissolution of the gas pockets inside the trenches must then be taken into account when calculating the filling time.

As the gas dissolves at the liquid front inside the trench and escapes from the trench by diffusion into the liquid, the amount of undissolved gas decreases and the liquid can continue to move towards the bottom of the trench.

The maximum filling time can then be estimated [8]. Interfacial phenomena, coupled with hydrodynamics, are involved in many industrial processes.

The viscosity of the liquid and the roughness of the surface influence the wetting properties. In a liquid, the dissipation of energy required to counteract the viscous friction affects the rate of spread of liquid on the solid.

4. Conclusion

This work focuses on the effect of pH on cleaning an antihistamine, fexofenadine, by two methods: rinsing and cleaning.

- The cleaning results showed that:
- The decrease in pH leads to a decrease in the cleaning efficiency.
- Fexofenadine hydrolyzes at a pH of less than 3.
- The free pH (4) of a solution of 100 mg / L fexofenadine gives a good cleaning performance with a percentage of 97.57%.

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