

## Protection of Environment by Extraction of $\beta$ -Naphthol from Cephalexin Exit Unit of Antibiotic Manufacture

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**Abstract.** The removal of  $\beta$ -naphthol from waste water of cephalexin exit unit of antibiotic manufacture in North of Iran has been studied. There are three organic and aqueous layers with waste  $\beta$ -naphthol that can cause water and environment pollution in process of synthesis, purification and crystallization of cephalexin. Acid-base extraction has been used by NaOH 5% and HCl 30% to obtain pure  $\beta$ -Naphthol (more than 98%) in good yield (93%).

**Keywords:** Cephalexin,  $\beta$ -Naphthol, Toxicity, Acid-Base Extraction, Antibiotic Manufacture

### 1. Introduction

Phenol is an important compound in petrochemical, pharmaceutical and several chemical industries [1]. Phenols are present in waste water of various industries, such as refineries, coking operations, coal processing, and manufacture of petrochemicals. Phenols are also the main organic constituents present in condensate streams in coal gasification and liquefaction processes. Other sources of waste water containing phenols are pharmaceutical, plastics, wood products, paint, and paper industries [2]. Phenols are pollutants of high priority concerns because of their toxicity and possible accumulation in the environments [3]. Due to the toxicity of phenolic effluents their treatment must be accomplished before the solutions can be safely discharged into the natural water resources. It has been found that phenol produces many adverse effects on fish and aquatic ecosystem when chronically exposed even at a small concentration [4]. In the past, toxic aromatic hydrocarbons were used for the recovery of phenols both in the laboratory and industrial scale. Recently several papers dealing with the feasibility of different separation processes to recover phenols have been published [5-12]. The aim of the present study is to remove  $\beta$ -naphthol from waste water of cephalexin exit unit of antibiotic manufacture In North of Iran with sodium hydroxide extraction method.

### 2. Results and Discussion

The Cephalosporin derivatives like cephalexin are important life saving antibiotics. Large-scale synthesis and purification of them from an aqueous solution is hampered by a number of problems. In manufactures purification and crystallization of cephalosporin can be achieved by adding  $\beta$ -naphthol to aqueous solution of them [13].

These derivatives selectively form complexes with  $\beta$ -naphthol that precipitate from an aqueous solution. In the crystalline state, the cephalosporins are less susceptible to degradation. Moreover, complexation provides a method for the isolation of the product, since the precipitated complex can be separated from the reaction mixture by simple filtration (Figure 1) [14].

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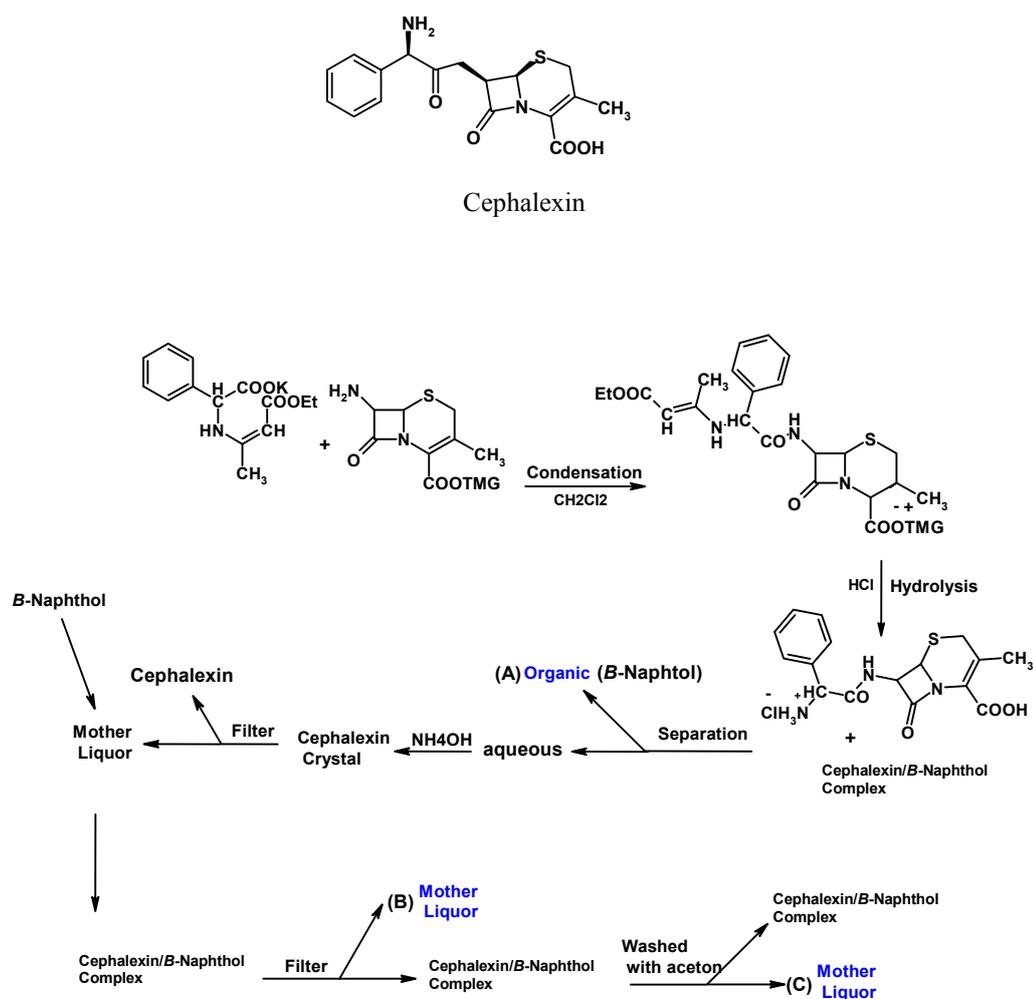


Fig. 1: process of synthesis, purification and crystallization of cephalexin

It is a well-known fact that  $\beta$ -Naphthol is aromatic compound and in class of phenolic derivatives.  $\beta$ -Naphthol is slightly soluble in water but its sodium salt is largely hydrolyzed and is soluble in water (Figure 2). This property permits it to transfer from organic layer to aqueous layer. According Scheme 1, it is necessary to remove  $\beta$ -Naphthol from organic layer (A), and wastewater {(B), (C)} to protect environment.

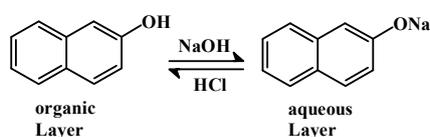


Fig. 2: Acid-base conjugated of  $\beta$ -Naphthol

-The first step was extraction of  $\beta$ -Naphthol from methylen chloride (A) by transfer it to separator funnel and washed with sodium hydroxide solution (5%), the extracted aqueous layer (D) was red and the progress of the extraction from organic layer was monitored by TLC using *n*-hexane–ethyl acetate (4:1) and the spots were visualized in UV light  $\lambda = 254$  &  $366$  nm.

- The second step was extraction of  $\beta$ -Naphthol from mother liquor (B). This is aqueous layer with  $\beta$ -Naphthol and, slightly other compounds like dimethyl acetamide (DMAC) and pyridine. It's better to separate  $\beta$ -Naphthol from other organic compounds, so this layer was washed with methylen chloride and then methylen chloride was washed with sodium hydroxide solution (5%) (Aqueous layer E). The extracted aqueous layer (E) was red and the progress of the extraction from organic layer was monitored by TLC.

- The 3th step was to remove acetone from aqueous layer (C) by evaporation under reduced pressure. At this point two layers (liquid & aqueous) formed to washed with methylen chloride to extract  $\beta$ -Naphthol (Cephalexin is slightly soluble in  $\text{CH}_2\text{Cl}_2$ ). Finally  $\beta$ -Naphthol was transferred from methylen chloride to aqueous layer by sodium hydroxide solution (5%) (Aqueous layer F).

-Three aqueous layers (D, E, & F) were mixed together and acidified by HCl (30%); all the time the temperature was controlled to be less than 18°C. The yellow brown precipitate was filtered, washed with water and dried to obtain pure  $\beta$ -Naphthol (more than 98% by HPLC, m.p 121- 122°C) in good yield (93%). It was ready to use for crystallization of cephalixin exit unit of antibiotic manufacture.

This acid-base  $\beta$ -naphthol extraction method is less expensive than other methods. Separation of waste  $\beta$ -naphthol reduces environmental pollution, reduces import material from foreign sources and can be used with the lowest cost producers in antibiotic manufacture. Organic solvents used in this separation method can be used again through recycling in the production of cephalixin, in addition sodium chloride or sodium hydroxide pollution in water is much less than  $\beta$ -naphthol.

### 3. Material and Methods

All of Chemical compounds and Solvents were purchased from Merck without further purification. TLC silica gel 60, aluminium sheets were purchased from Merck. The melting points were obtained using an Electrothermal IA 9100 Digital melting point apparatus. The IR spectra were recorded on a Bruker IFS-88 instrument (the samples as KBr disks for the range 4000–400  $\text{cm}^{-1}$ ).

#### 3.1. Extraction of $\beta$ -Naphthol from Methylen Chloride (A)

Organic layer (A) (165 ml) was washed with NaOH 5% (3x50 ml). The progress of the extraction from organic layer was monitored by TLC using *n*-hexane–ethyl acetate (4:1) and the spots were visualized in UV light  $\lambda = 254$  & 366 nm. Organic layer washed with NaOH 5% (3x80 ml). The aqueous layer (D) was separated, kept in 10-18 °C and acidified by HCl (30%)(15 ml), yellow brown precipitate was filtered, washed with water and recrystallized by ethanol: water (1:2), to obtain pure  $\beta$ -Naphthol (1.3g), m.p 121°C.

#### 3.2. Extraction of $\beta$ -Naphthol from Mother Liquor (B)

Mother liquor (B) (280 ml) was washed with methylen chloride (3x50 ml), The progress of the extraction from organic layer was monitored by TLC using *n*-hexane–ethyl acetate (4:1) and the spots were visualized in UV light  $\lambda = 254$  & 366 nm. The aqueous layer (E) was separated, kept in 10-18 °C and acidified by HCl (30%)(20 ml), yellow brown precipitate was filtered, washed with water and recrystallized by ethanol: water (1:2), to obtain pure  $\beta$ -Naphthol (1.8g), m.p 122°C.

#### 3.3. Extraction of $\beta$ -Naphthol from Aqueous Layer (C)

Aqueous layer (C) (15 ml) was concentrated by evaporation under reduced pressure to remove acetone. At this point two layers (liquid & aqueous) formed to wash with methylen chloride (30 ml). Organic layer was washed with NaOH 5% (3x30 ml). The aqueous layer (F) was separated, kept in 10-18 °C and acidified by HCl (30%)(18 ml), yellow brown precipitate was filtered, washed with water and recrystallized by ethanol: water (1:2), to obtain pure  $\beta$ -Naphthol (0.7g), m.p 122°C.

### 4. Acknowledgment

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