International Journal of Pharmacy Teaching & Practices 2013, Vol.4, Issue 3, 710-715.

# Foam Fractionation in Recovery of Congestive Heart Failure Drug (Captopril)

**Avishek Mandal**
M.Pharm (Pharmaceutical Engineering)
Jadavpur University,

**Research Article**

Please cite this paper as: Avishek Mandal. Foam Fractionation in Recovery of Congestive Heart Failure Drug (Captopril). IJPTP, 2013, 4(3), 710-715.

**Corresponding Author:**

**Avishek Mandal**
M.Pharm ( Pharmaceutical Engineering )
Jadavpur University,
Department Of Pharmaceutical Technology,Kolkata-700032
Email Id:-Avishek7477@Gmail.Com

## Abstract

In this study, the effects of some of the important parameters in foam fractionation (such as gas velocity, pH of feed solution, collector-colligend ratio, colligend concentration, feed volume, column height and aliphatic chain length of the collector) on the recovery of captopril were determined. Captopril (gifted by Wockhardt limited, Mumbai) was used throughout this research and Tablet Aceten (25 mg.) was purchased from local medicine shop. Tetradecyl trimethyl ammonium bromide (TDTMAB)(E. Merck India Limited), and hexadecyl trimethyl ammonium bromide (HDTMAB)(Loba Chemie, Bombay) were used as collectors. Other chemicals and reagents used were analytical reagent grade. For all experiments, double-distilled water was used. A schematic diagram of the apparatus used for batch process is shown in figure 1. A foam fractionation apparatus was uniquely designed and set up with glass works from glass blowing and supplements such as a gas cylinder for nitrogen supply and a flowmeter purchased from suppliers. Samples of the initial feed solution, of the foamate, as well as of the residual solution (for controlling purposes) were taken to determine the concentration of the drug. It was measured by the titrimetric assay method using starch solution as indicator. The results indicate that the percentage recovery of captopril in formulation was lower as compared to captopril in pure form from aqueous solution at $\varphi$ = 4. This is probably because of the presence of other soluble ingredients, which decreases the enrichment of captopril in formulation. As it is shown in Table V percentage recovery of captopril in pure form with TDTMAB (MW=336.40) was higher as compare to HDTMAB (MW = 364.46) at $\varphi$ = 4. Since the tendency of the collector to adsorb on the interface depends on the length of its aliphatic chain, investigation were carried out with quaternary ammonia salts, $RMe_3NBr$, where the aliphatic chain R consists of 14 and 16C- atoms. The longer the alkyl residue R, the lower the captopril concentration in the foam liquid. The results indicate that the lower the molecular weight of the surface-active agent gives higher percentage recovery.It is concluded that the experimental variables of SGV = 0.0541 cm/s, pH = 3.75, $\varphi$ = 4, $C_i$ = 0.5 mM/L, column height = 65cm gives highest percentage recovery of captopril from an aqueous solution by the foam fractionation method.

**Key words:** captopril, foam fractionation, CHF, drug discovery.

## INTRODUCTION

Captopril itself is relatively stable at temperatures up to 50°, and freely water-soluble anionic compound [1]. Captopril is a sulfhydryl containing dipeptide surrogate of proline. Captopril is the first orally active inhibitor of ACE. It is used in the treatment of severe essential and renovascular hypertension, where other therapy has failed, and congestive heart failure [2].

Foam fractionation is the foaming off of dissolved material from a solution via adsorption at the bubble surfaces. All methods of separation, whether physical or chemical, are based on differences in properties. The foam fractionation technique is based on the difference in surface activity. The surface active material, which may be molecular, colloidal, or macro particulate in size, is selectively adsorbed or attached at the surfaces of bubbles rising through the liquid, and is thereby concentrated or separated. A substance that is not surface active itself can sometimes be made effectively surface active through the deliberate addition, or presence otherwise, of a suitable surfactant (termed the collector), which will combine with the substance in question (termed the colligend) so that it may be adsorbed [3].

Foam fractionation applies a simple apparatus and causes only little investment, energy and running costs [4,5]. Foam fractionation devices can be run in a number of different modes: batch or continuous flow, with or without reflux of the

collapsed foamate, with or without multiple staging, with feed to a pool at the bottom of the column, or with feed into the rising foam [6]. Foam fractionation technique is especially effective for the separation of materials at low concentrations. Practically, foam is nevertheless formed in the micelle region and separations can be successfully carried out; however, better separation would occur below the CMC. Many factors affect the performance and efficiency of a foam separation system, the relative importance of each depending on the specific conditions [7].

The application of foam fractionation to biological materials, such as proteins, enzyme etc., is very much attractive [8-12]. Surfactants represent a striking problem in water resources. Foam fractionation enables both defoaming and concentration of surfactants [13]. Foam fractionation technique is important for the recovery of penicillin G at low concentration levels from aqueous solutions [14].

The fate of pharmaceuticals in aquatic environment has been recognized as one of the emerging issue in the environmental sciences. Presence of captopril can cause aquatic toxicity [15]. In this study, the effects of some of the important parameters in foam fractionation (such as gas velocity, pH of feed solution, collector-colligend ratio, colligend concentration, feed volume, column height and aliphatic chain length of the collector) on the recovery of captopril were determined.

## MATERIAL & METHODS

### Materials

Captopril (gifted by Wockhardt limited, Mumbai) was used throughout this research and Tablet Aceten (25 mg.) was purchased from local medicine shop. Tetradecyl trimethyl ammonium bromide (TDTMAB)(E. Merck India Limited), and hexadecyl trimethyl ammonium bromide (HDTMAB)(Loba Chemie, Bombay) were used as collectors. Other chemicals and reagents used were analytical reagent grade. For all experiments, double-distilled water was used.

### Foam fractionation

A schematic diagram of the apparatus used for batch process is shown in figure 1. A foam fractionation apparatus was uniquely designed and set up with glass works from glass blowing and supplements such as a gas cylinder for nitrogen supply and a flowmeter purchased from suppliers.

Glass column with an internal diameter 4.2 cm and length 65 cm was used in this study. The drug solution was contacted with the gas bubble rising from the frit (No. 3) fitted at the bottom of the column. The separation performance is referred to as the enrichment ratio ($E_r$) and percentage recovery ($R_p$) of captopril; the $E_r$ is the ratio of drug concentration in foamate versus the drug concentration in the initial feed solution, and $R_p$ is the percentage of the ratio of amount of drug in foamate and the amount of drug in the initial feed solution. A feed solution of desired concentration was prepared by dissolving pure drug with subsequent addition of required amount of surface-active agent. Formulated drug (tablet) was dissolved in sufficient amount of water in a conical flask and then solubilized the drug by the help of Ultrasonic cleaning bath for 15 minutes, then filter the solution with the help of whatman filter paper & then prepared the feed solution of desired concentration by dissolving surfactant. All the experiments were batch type. The feed solution were adjusted to the desired pH by using either by using either 0.1 M NaOH or 0.1 M HCL and then transferred to the column. Nitrogen gas was passed through the bottom of the column via a gas flowmeter and a humidifier. The surfactant form stable foam and drug was adsorbed on the foam-bubble interface. The foam was allowed to overflow the top of the column into a container and collapse into a small volume that is enriched with the drug. The concentration of initial feed solution and the residual solution and foamate (collapsed foam) were determined by the titrimetric assay method. All the experiments were performed in triplicate at room temperature and under atmospheric pressure.

### Analytical methods

Samples of the initial feed solution, of the foamate, as well as of the residual solution (for controlling purposes) were taken to determine the concentration of the drug. It was measured by the titrimetric assay method using starch solution as indicator [16].

### Calculation

The enrichment ratio ($E_r$) and percentage recovery ($R_p$) were calculated by the following equations:

Enrichment ratio ($E_r$) =Concentration of drug in the foam ($C_f$)/ Concentration of drug in the feed ($C_i$)

And Percentage recovery ($R_p$) =(Mass of drug in the foam/ Mass of drug in the feed) x 100

## RESULTS & DISCUSSION

Since Captopril cannot be enriched in the foam, collectors are needed. Two collectors with different chain length were used: Tetradecyl trimethyl ammonium bromide (TDTMAB, $C_{14}$ chain collector) & Hexadecyl trimethyl ammonium bromide (HDTMAB, $C_{16}$ chain collector).

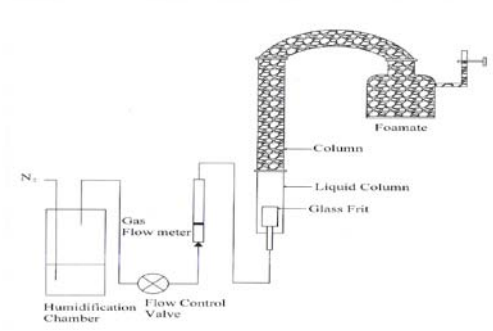


**Figure 1. Schematic diagram of foam fractionation apparatus.**

**Table I. Effect of superficial gas velocity, pH of feed solution and collector-colligend ratio on the recovery and enrichment of captopril in pure form**

| Concentration of TDTMAB (mM/L) | pH of the feed solution | SGV (cm/s) | Percentage recovery[a] | Enrichment ratio[b] |
|---|---|---|---|---|
| 1 | 3.75 | 0.0541 | 70.93 | 35.4648 |
| 1.5 | 3.75 | 0.0541 | 84.61 | 42.3048 |
| 2 | 1.50 | 0.0541 | 72.10 | 36.0520 |
| 2 | 2.25 | 0.0541 | 81.81 | 40.9066 |
| 2 | 3.00 | 0.0541 | 87.35 | 43.6726 |
| 2 | 3.75 | 0.0541 | 90.21 | 45.1082 |
| 2 | 3.75 | 0.0661 | 86.97 | 28.9900 |
| 2 | 3.75 | 0.0781 | 84.06 | 21.0156 |
| 2.5 | 3.75 | 0.0541 | 91.11 | 45.5560 |

[a] After 120 min of operation.
[b] When $C_i$ =0.5 mM/L, feed volume=100 ml, column height=65 cm.

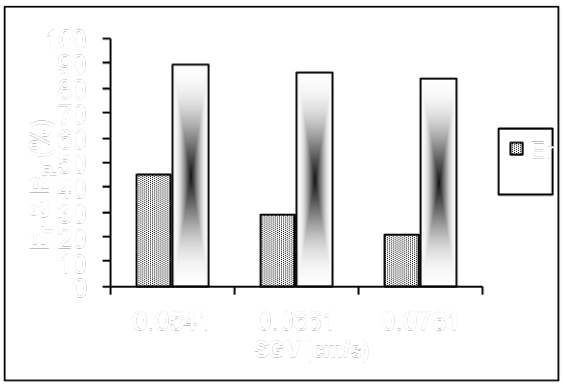


**Figure 2. Effect of SGV on $E_r$ & $R_p$ values of Captopril in pure form at pH= 3.75 ($C_i$ =0.5 mM/L, Time =120 mins, Conc.of TDTMAB=2mM/L, feed volume=100 ml, column height=65 cm).**

Figure 2 (Table I) shows the effect of superficial gas velocity (SGV) on the enrichment ratio ($E_r$) and percentage recovery ($R_p$) of captopril in pure form aqueous solution with TDTMAB. The results indicate that the values of enrichment ratio ($E_r$) and percentage recovery ($R_p$) of captopril in pure form decreased with the increasing of superficial gas velocity (SGV). Enrichment ratio and percentage recovery of captopril in pure form were found higher when superficial gas velocity (SGV) was 0.0541 cm/s in comparison to that of SGV 0.0661, 0.0781 cm/s. Amount of adsorbed material on the surface of the gas bubble depends on residence time of gas bubble in solution which in turn depends on low gas velocity. At SGV = 0.0541 cm/s, 90.21% of captopril in pure form is transferred into the foam with the help of TDTMAB (when Time = 120 mins, $\varphi$ = 4, pH = 3.75, $C_i$ =0.5 mM/L, Feed volume=100 ml, column height=65 cm).

**Table II. Effect of colligend concentration on the recovery and enrichment of captopril in pure form**

| $C_i$ (mM) | Percentage recovery[a] | Enrichment ratio[b] |
|---|---|---|
| 0.5 | 90.21 | 45.1082 |
| 0.75 | 82.16 | 41.0800 |
| 1 | 61.22 | 30.6112 |
| 1.25 | 58.88 | 29.4424 |

[a] After 120 min of operation.
[b] When concentration of TDTMAB=2 mM/L, pH of feed solution=3.75, SGV=0.0541 cm/s, feed volume=100 ml, column height=65 cm.

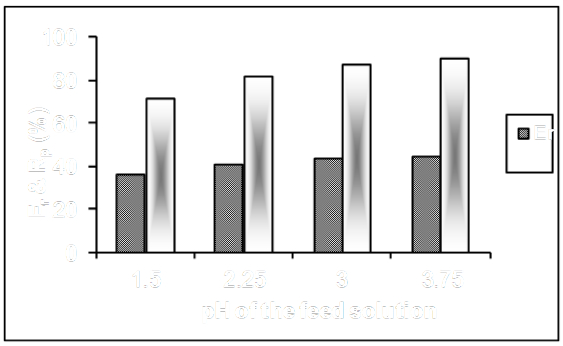


**Figure 3. Effect of pH of the feed solution on $E_r$ & $R_p$ values of Captopril in pure form (SGV=0.0541 cm/s, $C_i$ =0.5 mM/L, Time =120 mins, Conc.of TDTMAB=2mM/L, feed volume=100 ml, column height=65 cm).**

Figure 3 shows the effect of feed pH on the enrichment ratio ($E_r$) and percentage recovery ($R_p$) of captopril in pure form from aqueous solution. Enrichment ratio and percentage recovery of captopril in pure form were found higher when pH of feed was 3.75 in comparison to that of pH 1.5, 2.25 and 3. When pH of the feed solution is too low, the percentage recovery of captopril in pure form is less as because foam is less stable.

**Table III. Effect of feed volume on the recovery and enrichment of captopril in pure form**

| Feed volume (ml) | Percentage recovery[a] | Enrichment ratio[b] |
|---|---|---|
| 100 | 90.21 | 45.1082 |
| 200 | 50.93 | 40.7418 |
| 300 | 36.01 | 36.0074 |
| 400 | 31.23 | 35.6946 |
| 500 | 26.76 | 33.4460 |

[a] After 120 min of operation.
[b] When concentration of TDTMAB=2 mM/L, pH of feed solution=3.75, SGV=0.0541 cm/s, $C_i$ = 0.5 mM/L, column height=65 cm.

The main parameter was the collector-colligend ratio (φ). The collector alone cannot be flotated, but the collector captopril complex can. Figure 4 (Table I) shows the effect of collector - colligend ratio (φ) on the enrichment ratio ($E_r$) and percentage recovery ($R_p$) of captopril in pure form from aqueous solution. Percentage recovery of pure captopril was 90.21 with TDTMAB at φ = 4, provided time = 120 mins, SGV = 0.0541 cm/s and pH = 3.75. At φ = 5, percentage recovery of captopril in pure form with TDTMAB was almost similar (91.11%) to the recovery at φ = 4.

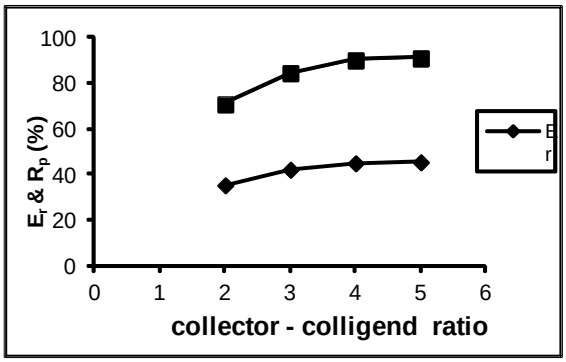


Figure 4. Effect of collector-colligend ratio on $E_r$ & $R_p$ values of Captopril in pure form at pH= 3.75 (SGV=0.0541 cm/s, $C_i$ =0.5 mM/L, Time =120 mins, feed volume=100 ml, column height=65 cm, SAA=TDTMAB).

**Table IV. Effect of column height on the recovery and enrichment of captopril in pure form**

| Column height (cm) | Percentage recovery[a] | Enrichment ratio[b] |
|---|---|---|
| 20 | 24.67 | 12.3383 |
| 35 | 31.58 | 15.7880 |
| 50 | 37.83 | 18.9148 |
| 65 | 90.21 | 45.1082 |

[a] After 120 min of operation.

[b] When concentration of TDTMAB=2 mM/L, pH of feed solution=3.75, SGV=0.0541 cm/s, $C_i$= 0.5 mM/L, feed volume=100 ml, column height=65 cm.

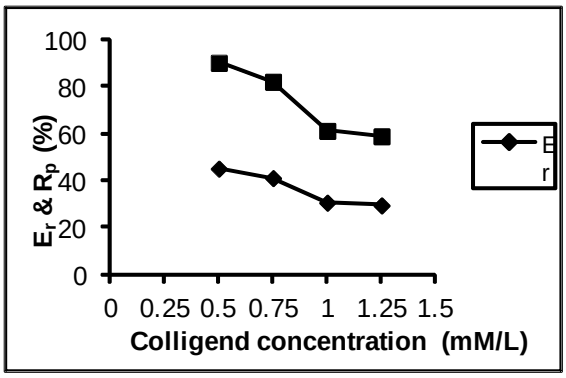


**Figure 5. Effect of Colligend concentration on $E_r$ & $R_p$ values of Captopril in pure form at pH = 3.75 (Time = 120 mins, SGV = 0.0541 cm/sec, Conc. of TDTMAB=2 mM/L, feed volume=100 ml, column height=65 cm).**

Figure 5 (Table II) shows the effect of colligend concentration on enrichment ratio ($E_r$) and percentage recovery ($R_p$) of captopril in pure form from aqueous solution at pH = 3.75. The results indicate that the enrichment ratio and percentage recovery of captopril in pure form decreases with the increasing concentration of the colligend. $E_r$ & $R_p$ values of captopril in pure form were found higher when colligend concentration was 0.5 mM/L in comparison to that of 0.75, 1 and 1.25 mM/L. This foam fractionation method is very much effective at lower concentration of feed.

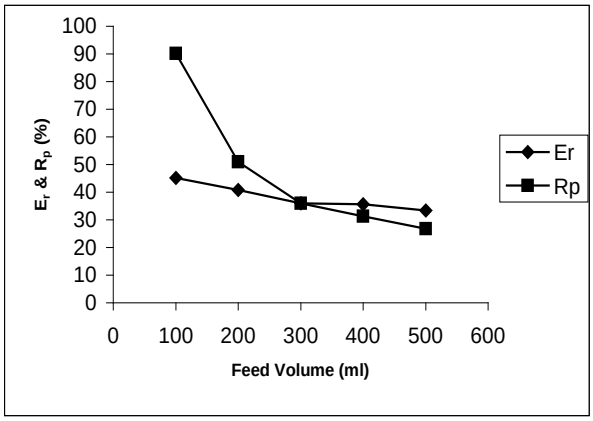


**Figure 6. Effect of Feed Volume on $E_r$ & $R_p$ values of Captopril in pure form at pH = 3.75 (Time = 120 mins, SGV = 0.0541 cm/sec, $C_i$ = 0.5 mM/L, Conc. of TDTMAB=2 mM/L, column height=65 cm).**

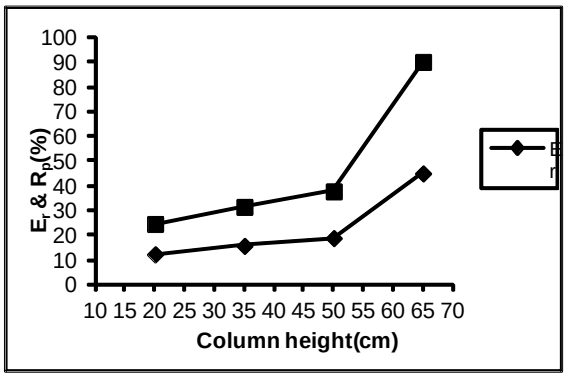


**Figure 7. Effect of Column height on $E_r$ & $R_p$ values of pure Captopril at pH = 3.75 (Time = 120 mins, SGV = 0.0541 cm/sec, $C_i$ = 0.5 mM/L, Conc. of TDTMAB=2 mM/L, feed volume=100 ml).**

**Table V. Effect of aliphatic chain length of the collector on the recovery and enrichment of captopril**

| | Concentration of SAA (mM/L) | Percentage recovery[a] | | Enrichment ratio[b] | |
|---|---|---|---|---|---|
| | | Captopril in pure form | Captopril in formulation | Captopril in pure form | Captopril in formulation |
| SAA, TDTMAB | 2 | 90.21 | 81.66 | 45.1082 | 40.8312 |
| SAA, HDTMAB | 2 | 83.85 | 73.9 | 41.9256 | 36.9524 |

[a] After 120 min of operation

[b] When, pH of feed solution=3.75, SGV=0.0541 cm/s, $C_i$= 0.5 mM/L, feed volume=100 ml, column height=65 cm.

Figure 6 (Table III) shows the effect of feed volume on the enrichment ratio and percentage recovery of captopril in pure form from aqueous solution with TDTMAB at pH = 3.75. The results indicate that the enrichment ratio and percentage recovery decreases with the increasing feed volume. When feed volume is less, in that case there is a sufficient foam height inside the column, and it provides dry foam, therefore enrichment ratio and the percentage recovery is high.

As it is shown in Figure 7 (Table IV), the enrichment ratio and percentage recovery of captopril in pure form increases as the column height increases, presumably due to the development of dry foam with the increasing column height.

The results (Table V) indicate that the percentage recovery of captopril in formulation was lower as compared to captopril in pure form from aqueous solution at $\varphi$ = 4. This is probably because of the presence of other soluble ingredients, which decreases the enrichment of captopril in formulation. As it is shown in Table V percentage recovery of captopril in pure form with TDTMAB (MW=336.40) was higher as compare to HDTMAB (MW = 364.46) at $\varphi$ = 4. Since the tendency of the collector to adsorb on the interface depends on the length of its aliphatic chain, investigation were carried out with quaternary ammonia salts, $RMe_3NBr$, where the aliphatic chain R consists of 14 and 16C- atoms. The longer the alkyl residue R, the lower the captopril concentration in the foam liquid. The results indicate that the lower the molecular weight of the surface-active agent gives higher percentage recovery.

## CONCLUSION

It is concluded that the experimental variables of SGV = 0.0541 cm/s, pH = 3.75, $\varphi$ = 4, $C_i$ = 0.5 mM/L, column height = 65cm gives highest percentage recovery of captopril from an aqueous solution by the foam fractionation method. It is also concluded that for 100ml feed volume, 90.21% of captopril recovered with TDTMAB at SGV=0.0541 cm/s (when $\varphi$ = 4). The results also proved that low molecular weight & moderate chain length of surface-active agent (tertadecyl trimethyl ammonium bromide) gives maximum percentage recovery of captopril than with hexadecyl trimethyl ammonium bromide. It is suggested that the removal amount can be enhanced by increasing the height of the liquid column and column height and adding more SAA initial and at intervals.

## References

[1] Martindale, The Extra Pharmacopoeia, Thirty first ed., Royal Pharmaceutical Society, London, 1996, pp. 838.

[2] K. D. Tripathi, Essentials of Medical Pharmacology, Fifth ed., Jaypee Brothers Medical Publishers (P) Ltd., New Delhi, 2003.

[3] R. Lemlich, Adsorptive Bubble Separation Technique, Academic press, New York, 1972.

[4] F. Uraizee, G. Narsimhan, Foam fractionation of proteins and enzymes-II. Performance and modeling, Enzyme Microb. Technol. 12 (1990) 315-316.

[5] A. K. Brown, A. Kaul, J. Varley, Continuous foaming for protein recovery I. Recovery of β-casein, Biotechnol. Bioeng. 62 (1999) 278-290.

[6] Ann N. Clarke, D. J. Wilson, Foam Flotation: Theory and Applications, Marcel Dekker Inc., New York and Basel, 1983.

[7] P. A. Schweitzer, Handbook of separation Techniques for chemical engineers, Mc. Graw -Hill Inc., United states of America, 1979.

[8] C. E. Lockwood, Michael Jay, Paul M. Bummer, Foam Fractionation of Binary Mixtures of Lysozyme and Albumin, Journal of Pharmaceutical sciences, 89 (2000) 693-704.

[9] Zaid S. Saleh, Md. M. Hossain, A study of the separation of proteins from multicomponent mixtures by a semi-batch foaming process, Chemical Engineering and Processing, 40 (2001) 371-378.

[10] Akira Suzuki, Kazuki Yasuhara, Hideshi Seki, Hideo Maruyama, Selective Foam Separation of binary protein solution by SDS complexation method, Journal of Colloid and Interface Science, 253 (2002) 402-408.

[11] V. Burapatana, A. Prokop, Robert D. Tanner, A comparison of the activity reduction occurring in two detergent-assisted protein (cellulase and lysozyme), Separation Science and Technology, 40 (2005) 2445 – 2461.

[12] Brite M. Gerken, Andreas Nicolai, Diana Linke, Holger Zorn, Ralf G. Berger, Harun Parlar, Effective enrichment and recovery of laccase C using continuous foam fractionation, Separation and Purification Technology, 49 (2006) 291-294.

[13] Andrej Sonc, Viktor Grilc, Batch foam fractionation of surfactants from aqueous solutions, Acta Chim. Solv. 51 (2004) 687-698.
[14] Ralf Dieter Gehle, Karl Schugerl, Penicillin recovery from aqueous solutions by continuous foam flotation, Appl. Microbiol. Biotechnol. 19 (1984) 373-375.
[15] Grzegorz Nalecz- Jawecki, Guido Persoone, Toxicity of Selected pharmaceuticals to the Anostracan Crustacean *Thamnocephalus platyurus*, Environ. Sci. & Pollut. Res. 13 (2006) 22 – 27.
[16] Indian Pharmacopoeia, Vol. 1, Controller of Publication, Civil lines Delhi – 110054, 1996.

## AUTHORS' CONTRIBUTIONS

Authors contributed equally to all aspects of the study.

## PEER REVIEW

Not commissioned; externally peer reviewed.

## CONFLICTS OF INTEREST

The authors declare that they have no competing interests.