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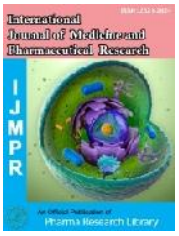

Research Article **Open Access**

Formulation and Evaluation of Ceftibuten Dry Syrup

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A B S T R A C T

Drugs are most important part which have to be developed in to an acceptable dosage form. They preferred when drug stability is a major target. In present study solid dispersion technique was used for taste masking and dissolution enhancement. It has been defined as dispersion of one or more active ingredients in an inert carrier with solvent evaporation method used. In this study Ceftibuten taste was masked by using *Eudragit EPO* and stearic Acid polymer in 1:1 ratio. Taste masking generally achieved with solid dispersion technique. In which the taste of the final formula were evaluated from human volunteers and grades were given according to the taste of the final formulation.

Keywords: Ceftibuten, Taste masking, Dissolution, solid Dispersion Technique, Dry syrup.

A R T I C L E I N F O

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1. Introduction

Oral administration of bitter drugs is important issue for health care providers especially with pediatrics and geriatric patient. Drugs are most important part which have to be developed in to an acceptable dosage form. The factors which affect selection of taste masking technology is extent of unpleasant taste, dose of active pharmaceuticals, drug particle shape and size distribution, dosage forms, drug solubility, ionic characteristics of the drug. Nearly 70% preparation are available in market are solid form composed of tablet, capsule and powder i.e. dry syrup, effervescent powder, powder for topical use, powder for injection etc. These dosage forms are designed either for improving the physical and mechanical properties of materials during manufacture. The drug stability is a major target. Taste maskings of the drug based on the formulation of the dosage forms are–coating, granulation, sweeteners microencapsulation, taste suppressants and potentiators, solid dispersions etc. while solid dispersion is most efficient

and commonly used due to its ease of formulation. It has been defined as dispersion of one or more active ingredients in an inert carrier or matrix at solid state prepared by melting solvent method. The solid dispersion mostly formulated with solvent evaporation method. In which both drug and carrier are dissolved inorganic solvent. After entire dissolution, the solvent is evaporated. The solid mass is ground, sieved and dried.

2. Materials and Methods

Materials

The formulation drug and excipients used are *Ceftibuten* sample by Covalent Laboratories Pvt. Ltd. Hyderabad, *Eudragit EPO* by Evonik Degussa India Pvt.Ltd. Mumbai, β-cyclodextrin by Sequent Scientific Ltd. Bangalore. All other ingredients viz. methylcellulose, ethyl cellulose, steric acid by Covalent Laboratories Pvt. Ltd. Hyderabad.

Pre Formulation Methods:

Compatibility study for excipients with drug determination of λ max.

Determination of λ max:

λmax determined of ceftibuten with glycin buffer pH 5.5. the concentration to obtain 20 µg/ml with glycin buffer. The Uv spectrum was recorded in the range 700-800nm. The wavelength of maximum absorption (λ max) was found from the scan using double beam UV visible spectrophotometer.

Phase Solubility Studies:

Solubility measurements were performed. In this excess amount of drug of about 100mg was added to 25ml glycine buffer pH 5.5 containing increasing concentrations of the polymer (I.e. 1%,2%, 3%, 4%,5%,6% w/v). it was sealed and shaken at room temperature after filtered through whatman filter paper filtrate was suitably diluted and analyzed at uv- visible spectro photometrically at specified wavelength.

Preparation of standard curve of ceftibuten:

Calibration curve was plotted with 5.5 pH glycin buffer at λmax 798 nm using Uv-visible spectrophotometer. The serial dilution of 5,10,15,20,25 µg/ml were prepared in buffer. The absorbance taken in triplicate its averages taken as values for standard calibration curve.

Pre-Treatment studies of the resin:

The resin treated with deionised water and alcohol to remove the impurities. The resultant resin was dried and further used as excipient.

Preparation of Drug: Resin complex: The polymers were used are Eudragit EPO, methyl cellulose, ethyl cellulose & β-cyclodextrin. The solid dispersion prepared with solvent evaporation method. The drug and polymer ratio fixed as 1:1 with that of phase solubility study for all polymers. The complexin which polymers are divided with stearic acid and polymerequally. Which further designed with a ratio that is 1:0.5, 1:1 by keeping polymer concentration constant and stearic acid concentration varied. This blend dissolved in acetone with constant stirring and allowed to evaporate on aluminium foil covered petriplate up to complete dryness. The dried powder complex was stored in air tight container.

Evaluation of complex drug:

Pre formulation studies of powder blend:

The prepared powder blend was subjected to preformulation studies like angle of repose, bulk density, tapped density, carr'sindex and hausner ratio.

Drug content:

To determine actual drug content per unit weight of the drug polymer complex. The specific weight of complex was evaluated with pH 5.5 glycine buffer and analyzed at 798 nm on UV visible spectrophotometer.

Development of Dry Syrup Formulation

All the ingredients were accurately weighed and complex drug was sifted through #40 mesh with other excipients excluding flavor. Flavor was sifted separately. All mixtures were loaded for blending for 10 min to ensure complete mixing. After mixing of all the ingredients were filled into the closed container as primary storing container and sealed.

Evaluation of Dry Syrup:

In-Vitro Dissolution Studies:

Single dose of reconstitute syrup were studied for in vitro dissolution using type II dissolution testing apparatus. The media used were glycine buffer pH5.5 with speed 75 rpm and at 37±0.5 ºC duration of study was 60 min. absorbance was measured at 798 nm by uv spectro photometer.

Sedimentation Volume (F):

Sedimentation volume (F) is a ratio of the final or ultimate volume of sediment (Vu) to the original volume of sediment (Vo) before settling. It can be calculated by following equation

$$F=Vu/Vo$$

Where, Vu= final/ ultimate volume of sediment
Vo=original volume of suspension before settling

Taste Evaluation:

Panel method or sensory method:

The optimized formulation and ceftibuten were subjected to taste evaluation on human volunteers. Classifying bitter unpleasant taste.

3. Results and Discussion

Pre-formulation studies:

Determination of max:

Absorption maxima of ceftibuten in glycine buffer pH5.5 were estimated in UV spectrophotometer was found to be 798nm.

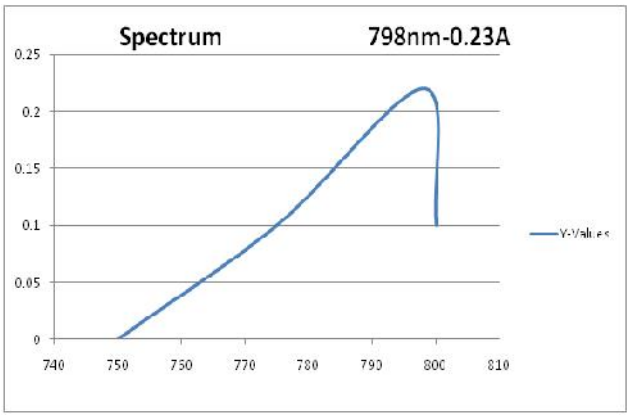

Figure 1: UV spectra of ceftibuten

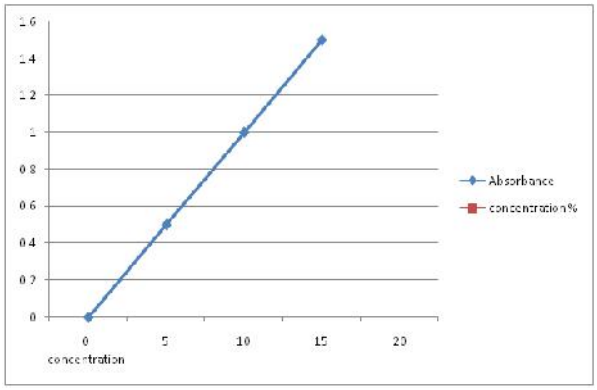

Figure 2: Phase solubility study of Eudragit EPO and Ceftibuten

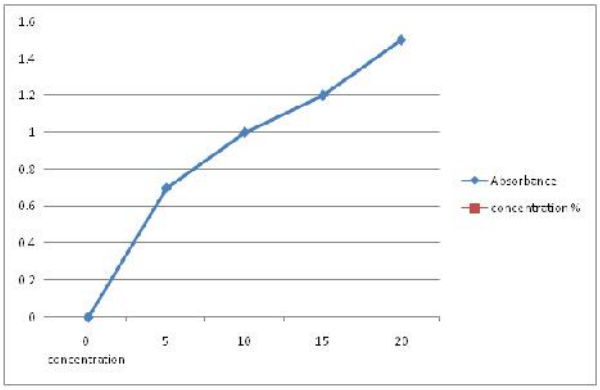

Figure 6: Phase solubility study of steric Acid and Ceftibuten

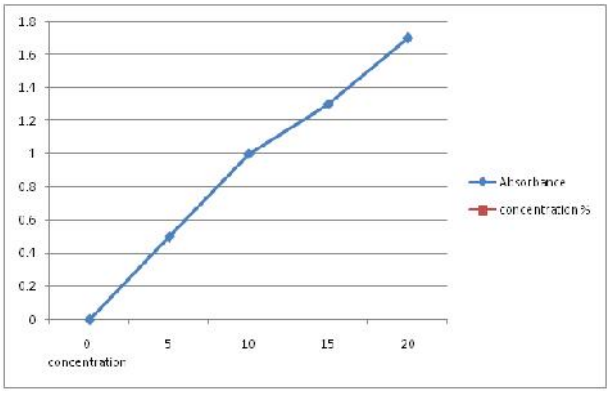

Figure 3: Phase solubility study of β-cyclodextrin and Ceftibuten

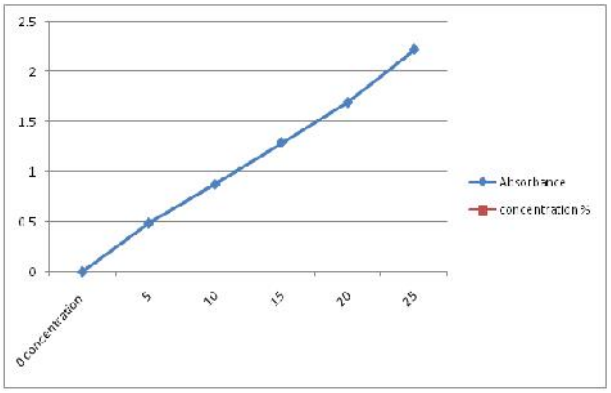

Figure 7: Evaluation of active pharmaceutical ingredient & polymer complex

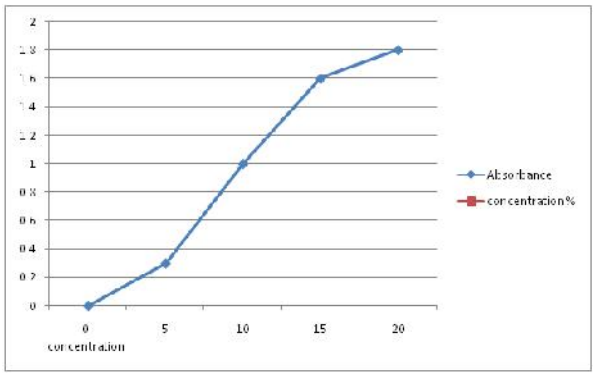

Figure 4: Phase solubility study of ethyl cellulose and Ceftibuten

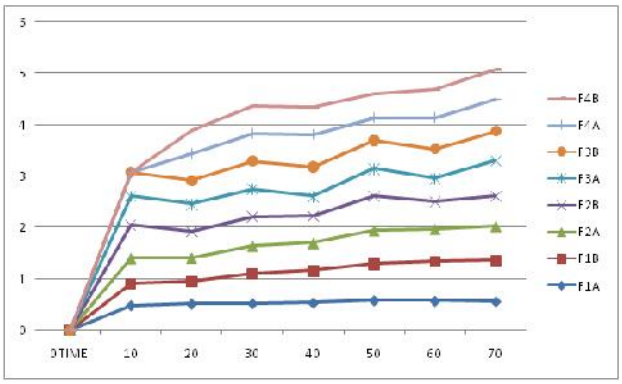

Figure 8: Drug with Complex of Eudragit

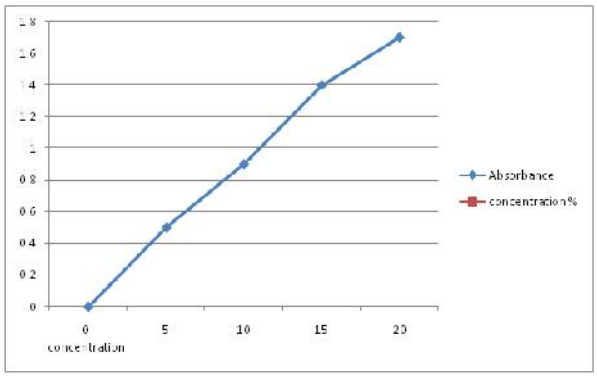

Figure 5: Phase solubility study of methyl cellulose and Ceftibuten

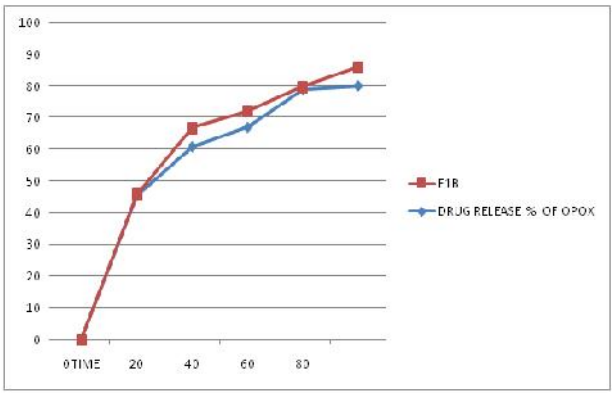

Figure 9: The rate of in-vitro drug release of marketed opaxy dry syrup 50 mg was lower than optimized batch.

Pre- formulation study of powder blend:

The evaluation of various powder blend was performed with regarding to bulk density, tapped density, carr's index, Hausner's ratio and Angle of repose was performed for the prepared powder blend of all batches and results were indicated. The results os all these tests were complied with specification in I.P. standards.

Drug content: The drug- polymer complexes prepared by solvent evaporation method in ratio of 1:05, 1:1 were subjected to content uniformity. The percent of drug present in each ratio. This indicated that, the drug contents are within limit of official compendia.

Evaluation of Dry Syrup:

In-vitro dissolution studies:

Dissolution of each of the complex was carried out to observe the release pattern of the drug from the complex. Dissolution of drug was also carried out to compare with release pattern of the drug with the complex. The dissolution studies were carried out in glycine buffer pH5.5.

4. Conclusion

The present research work was an attempt to study systematically, the effect of formulation variables on the release properties and taste masking of ceftibuten. Complex preparation ratio was selected on the phase solubility studies. For selection of formulation ratio, phase solubility studies were carried out in that all polymer with drug gave an linear proportion i.e 1:1. Hence 1:1 drug polymer ratio was considered for taste masking. The drug resin complex show good taste masking property for ceftibuten with Eudragit EPO and steric acid in 1:1 ratio. The prepared dry syrup of ceftibuten formula -1B showed good taste. The release profile of optimized formulation 1B of ceftibuten dry syrup was better as compared to marketed formulation.

Table 1: Formulation and preparation of dry syrup

Batches ingredients (mg)	Formula -1A 500mg	Formula -1A 100mg	Formula -1B 500mg	Formula -1B 100mg
Ceftibuten	12	2.4	12	2.4
Eudragit EPO	6	1.2	6	1.2
Stearic acid	3	0.6	6	1.2
Sodium benzoate	12	2.4	12	2.4
Sodium Saccharin	96.5	19.3	97	19.4
Xanthum gum	24	4.8	25	5.0
Aerosol	9.5	1.9	10	2.0
Talc	12	2.4	12	2.4
Flavor	q.s	q.s	q.s	q.s
Lactose	108.5	21.7	105	21.0
Pharma grade sugar	216.5	43.3	215	43

Table 2

Batches ingredients (mg)	Formula -2A 500mg	Formula -2A 100mg	Formula -2B 500mg	Formula -2B 100mg
Ceftibuten	12	2.4	12	2.4
Methyl cellolose	6	1.2	6	1.2
Stearic acid	3	0.6	6	1.2
Sodium benzoate	12	2.4	12	2.4
Sodium Saccharin	96.5	19.3	97	19.4
Xanthum gum	24	4.8	25	5.0
Aerosol	9.5	1.9	10	2.0
Talc	12	2.4	12	2.4
Flavor	q.s	q.s	q.s	q.s
Lactose	108.5	21.7	105	21.0
Pharma grade sugar	216.5	43.3	215	43

Table 3

Batches ingredients (mg)	Formula -3A 500mg	Formula -3A 100mg	Formula -3B 500mg	Formula -3B 100mg
Ceftibuten	12	2.4	12	2.4
Ethyl cellulose	6	1.2	6	1.2
Stearic acid	3	0.6	6	1.2
Sodium benzoate	12	2.4	12	2.4
Sodium Saccharin	96.5	19.3	97	19.4
Xanthum gum	24	4.8	25	5.0

Aerosol	9.5	1.9	10	2.0
Talc	12	2.4	12	2.4
Flavor	q.s	q.s	q.s	q.s
Lactose	108.5	21.7	105	21.0
Pharma grade sugar	216.5	43.3	215	43

Table 4

Batches ingredients (mg)	**Formula -4A 500mg**	**Formula -4A 100mg**	**Formula -4B 500mg**	**Formula -4B 100mg**
Ceftibuten	12	2.4	12	2.4
β-cyclodextrin	6	1.2	6	1.2
Stearic acid	3	0.6	6	1.2
Sodium benzoate	12	2.4	12	2.4
Sodium Saccharin	96.5	19.3	97	19.4
Xanthum gum	24	4.8	25	5.0
Aerosol	9.5	1.9	10	2.0
Talc	12	2.4	12	2.4
Flavor	q.s	q.s	q.s	q.s
Lactose	108.5	21.7	105	21.0
Pharma grade sugar	216.5	43.3	215	43

Table 5: Standard calibration curve of ceftibuten

S.NO	**CONCENTRATION(µ/ML)**	**ABSORBANCE**
1	0	0
2	5	0.486
3	10	0.8707
4	15	1.2894
5	20	1.6903
6	25	2.2184

Table 6: Pre- formulation study of powder blend

Formulations	**Angle of repose ±SD (degree)**	**Bulk Density ±SD (gm/ml)**	**Tapped density ±SD (gm/ml)**	**Hausner's Ratio**	**Carr's Index%**
F1A	27.94±1.5	0.46±0.21	0.54±0.11	1.17	14.81
F1B	2.6.98±0.69	0.56±0.14	0.45±0.15	1.15	11.20
F2A	32.89±0.24	0.54±0.14	0.65±0.17	1.20	16.11
F2B	29.98±0.27	0.43±0.33	0.49±0.14	1.18	14.76
F3A	35.25±0.56	0.45±0.014	0.57±0.02	1.22	19.23
F3B	34.53±0.29	0.47±0.12	0.58±0.61	1.25	18.16
F4A	30.43±1.25	0.49±0.37	0.52±1.35	1.19	16.29
F4B	31.36±1.26	0.62±0.34	0.47±1.47	1.21	22.37

Table 7: Evaluation of drug content

Resin	Resin to drug ratio	Drug content(%)
EUDRAGIT EPO	1:0.5	90.46
	1:1	99.96
β-cyclodextrin	1:0.5	87.43
	1:1	82.68
METHYL CELLULOSE	1:0.5	78.34
	1:1	77.96
ETHYL CELLULOSE	1:0.5	79.20
	1:1	92.78

Table 8: Cumulative % In-vitro Drug release profile of formulation

Time Min	F1A	F1B	F2A	F2B	F3A	F3B	F4A	F4B
0	0	0	0	0	0	0	0	0
5	0.51±0.24	0.44±0.12	0.46±0.13	0.51±0.10	0.53±0.16	0.46±0.13	0.53±0.15	0.46±0.16
10	0.52±0.44	0.58±0.15	0.54±0.54	0.57±0.40	0.54±0.56	0.54±0.83	0.54±0.54	0.54±0.36
20	0.53±0.36	0.63±0.32	0.54±0.36	0.53±0.01	0.37±0.24	0.57±0.56	0.64±0.66	0.54±0.21
30	0.58±0.04	0.71±0.33	0.65±0.54	0.67±0.06	0.53±0.07	0.55±0.06	0.45±0.07	0.47±0.05
40	0.57±0.52	0.77±0.045	0.63±0.10	0.54±0.23	0.45±0.46	0.57±0.75	0.61±0.55	0.55±0.64
50	0.56±0.6	0.80±0.42	0.67±0.37	0.58±0.38	0.69±0.65	0.57±0.37	0.63±0.35	0.58±0.38

Table 9: In-vitro drug release study of marketed formula and optimized batch

Time (min)	**Opox Dry Syrup 50mg**	**Formula F1b**
0	0	0
5	45.39±0.53	0.44±0.12
10	60.77±0.44	0.58±0.15
20	66.85±11	0.63±0.32
30	78.97±1.07	0.71±0.33
40	79.95±1.67	0.77±0.045
50	81.06±0.54	0.80±0.42

Table 10: Sedimentation volume

Parameter	F1A	F1B	F2A	F2B	F3A	F3B	F4A	F4B
Sedimentation volume	0.91	0.97	0.89	0.87	0.91	0.94	0.86	0.88

Table 11: Evaluation of taste by panel test

RESIN	**Resin To Drug Ratio (Polymer: Drug)**	**Class given by panel**
Eudragit EPO	1:0.5	3
	1:1	4
β-cyclodextrin	1:0.5	5
	1:1	3
Methyl Cellulose	1:0.5	4
	1:1	3
Ethyl cellulose	1:0.5	4
	1:1	3

5. References

[1] Yuveraj Singh Tanwar, Pushpendra Singh Naruka, Garima Rani Ojha Development and evaluation of floating microspheres of verapamil hydrochloride Revista Brasileira de Ciências Farmacêuticas ,Brazilian Journal of Pharmaceutical Sciences. 2007, 43(4).

[2] Singh Bandana,Kanoujia Jovita, Pandey Manisha, Saraf Shubhini A. Formulation and Evaluation of Floating Microspheres of Famotidine International Journal of Pharm Tech Research, 2010, 2(2):1415-1420.

[3] Mukesh P. Ratnaparkhi, Suresh B. Dhiwar, KiranE. Dhage,Sharvari S. Bhore, Pratiksha M. Kadamand Pradeep S. Patil Formulation and in-vitro characterization of floating microspheres of Metfomin HCl Scholars Research Library Der Lettre, 2014 (5):1390-1400

[4] S.K. Senthilkumar, B.Jaykar, S.Kavimani, Formulation, Characterization &In-vitroEvaluation of Floating Microsphere Containing Rabeprazole Sodium, JITPS 2010, 1(6), 274-282.

[5] Singh Bandana,Kanoujia Jovita, Pandey Manisha, Saraf Shubhini A. Formulation and Evaluation of Floating Microspheres of Famotidine International Journal of Pharm Tech Research, 2010, 2(2):1415-1420.

[6] Mukesh P. Ratnaparkhi, Suresh B. Dhiwar, KiranE. Dhage,Sharvari S. Bhore, Pratiksha M. Kadamand Pradeep S. Patil Formulation and in-vitro characterization of floating microspheres of Metfomin HCl Scholars Research Library Der Lettre, 2014 (5):1390-1400

[7] V. Sai Kishore, B. Tejeswara Rao, K. Pavani, D.Nagasen, K. Rakesh Varma and D. Gowtham Plantago Ovata Seeds and Bhringaraj Leaves As Superdisintegrants: Formulation And Evaluation of Sotalol Hydrochloride Orodispersible Tablets, IJPCBS 2013, 3(4), 1040- 1046.

[8] Upadhyayl.K.- Formulation And Evaluation of Dry Syrup Containing Bitter Drug –Pelagia Research Library Der Pharmacia Sinica, 2016, 7(4):64-72.

[9] Sonawane V.M., Shinde N.Y., Der Pharmaciahiguchi T and Connors KA, Phase-Solubility Techniques. Adva Anal Cheminstr, Letter, 2010,2(6):1-15
[10] Higuchi T and Connors KA, Phase- Solubility Techniques. Adva Anal Cheminstr, 1965,4: 212-217
[11] Felton LA., Remington Essentials Of Pharmaceutics, Pharmaceutical Press, 2012, Page No: 320-321
[12] Wagh V.D. journal of pharmacy research 2009,2(6), page no: 1049-1054
[13] Gupta.S.C Khambeta H. SUdhakar CK., Jain .S., journal of chemical & pharmaceutical research 2011, 3(4), page no :55-61
[14] United states pharmacopeia 30/NF 27 The official compendia of standards 2007
[15] Suthar A.M., Patel M.M., International journal of Applied pharmaceutics, Volume-3,2011, page no:16-19
[16] Kemp S.E., Hollowood T., Hortj., Sensory Evaluation A partical handbook, Ajohn Wiley &sons, Ltd. Publication, 2009, page no : 66-136 .