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PREPARATION AND CHARACTERIZATION OF FEW MALODOR MASKED NUTRIENTS

S. P. Ahire[1]*, P. P. Ahire[2], A. G. Zalte[1], V. S. Gulecha[1]
[1]School of Pharmaceutical Sciences, Sandip University, Nashik, Maharashtra.
[2]Alembic Pharmaceuticals Ltd., Karakhadi, Vadodara, Gujarat.
Email: shubhamahire7@gmail.com

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Abstract

"The worse the taste or odor of the medication, the better the cure", was once the prevailing attitude. Today, changes in patient attitude and the development of numerous flavoring agents have reversed that opinion. Patients now expect and demand medications that are pleasantly, or at least tolerably, flavored. This is especially true with children to whom this are most often prescribed. In other words, an unpleasant odor in a formulation reduces patient acceptance, preference, and compliance for olfactory properties and there is no proper measurement technique/method for the same. So, it is very challenging to assess the odors and their evaluations. The selection of the nutrient is based on the odor and nutritional functions of the nutrients. Two methods for odor evaluation including Electronic nose method and sensory method. The electronic nose method is there but it is not the cost effective method and also not globally accepted. Subjectively direct rating for intensity or hedonic tone by sensory method is easier and cheaper method. Highly accurate methods are not always necessary, so sensory method is most convenient one. Particle coating is the process by which very tiny droplets or particles of liquids or solids material are coated with a continuous film of polymeric material can change the property of target particle. Mostly in powder particle coating process, the solution of coating is used. The pan coating process is the oldest industrial procedures for forming small, coated particles or tablets.

Keywords: Amino Acids, Pan Coating, Odour, DSC.

1. Introduction

Amino acids are biologically important organic compounds composed of amine and acid functional, along with a side-chain specific to each amino acid. The key elements of an amino acid are carbon, hydrogen, oxygen, and nitrogen, though other elements are found in the side-chains of certain amino acids. When taken up into the human body from the diet, the 22 standard amino acids either are used to synthesize proteins and other biomolecules or are oxidized to urea and carbon dioxide as a source of energy.Aside from playing an important role in protein and enzyme synthesis, amino acids are considered very crucial for good health, since they contribute to the health of the human nervous system, hormone production, and muscular structure.In addition, they are needed for vital organs and cellular structure. If a person experiences low levels of the essential amino acids, this may cause hormonal imbalances, lack of concentration, irritability, and even depression

Formulations in the pharmaceutical field have three characteristics: physical characteristics such as size, hardness, friability, disintegration, and dissolution; chemical characteristics such as drug contents and stability of drugs; and sensory characteristics such as appearance, taste, and odor. Among these three characteristics, sensory characteristics are the characteristics which patients initially recognize, and of the sensory characteristics odor is one of the most important in patient acceptance, preference, and compliance for formulations. In other words, an unpleasant odor in a formulation reduces patient acceptance, preference, and compliance. Some symptoms that odor-producing chemicals may cause subjective symptoms like headache, dizziness, nausea, light headed, Visible signs like watery, itchy or burning eyes, burning nose or throat, Coughing and wheezing, Increased heart rate and Emotional effects like mood and behavior changes, depression and sadness, fear, annoyance and stress. There are mainly two methods for odor evaluation i.e. Instrumental method (Electronic nose) and sensory method. The electronic nose method is there but it is not the cost effective method and also not globally accepted. Subjectively direct rating for intensity or hedonic tone by sensory method is easier and cheaper method. Highly accurate methods are not always necessary, so sensory method is most convenient one.

The objective of the study was to develop a formulation of coated Non pelleted seeds (for odor masking) which are expected to mask the objectionable odor of the amino acids, improve patient compliance and convenience and develop proper method of formulation.

2. Material and Method

2.1 Material

N-Acetyl L-Cysteine was received as a gift sample from the Sami Labs Ltd, Kunigal, Karnataka, India. Other ingredients and solvents were obtained from different commercial suppliers.

2.2 Preparation of coated NPS (Non Pelleted Seeds)

In the present study, the trials are taken to mask the odour of the nutrients. These are prepared by mixing the API with the base material in various weight proportions. The suitable polymeric agent and the flavor was also added. The polymeric solution is prepared in water as a solvent and homogenized for 15 to 20 min. by using magnetic stirrer. The flavor was added as required. The following table gives the various weight proportions of the compositions listed above. The further procedure of coating had been done by using Pan Coater.

Table no.1: Formulation of trial batches of API.

Trial Batch No	**Active (gm)**	**Loading base (gm)**				**Polymers (gm/ml)**			**Flavors (gm/ml)**	
	API	Sugar	Maltodextrin	DCP	Starch	Na-CMC	Guar gum	HPMC LV-100	Orange	Chocolate
1	40	-	15	15	30	0.1	-	-	0.3	-
2	50	5	15	15	20	0.2	-	-	-	-
3	55	5	15	-	25	0.1	-	-	-	
4	55		15	10	20	0.2	-	-	-	-
5	55	5	25	-	15	-	0.3	-	-	
6	60	-	25	-	15	0.2	-	-	-	-
7	65	-	25	5	5	0.1	-	-	0.2	-

8	70	5	25	10	20	0.1	-	2.5	-	-
9	75		25	-	-	0.1	-	-		0.5
10	75		25	-	-	0.2	-	-	-	0.1
11	75	-	23	2	-	0.2	0.3	-	0.2	-

3. Preliminary Characterization

3.1 Drug-polymer compatibility study by FT-IR spectrophotometer

This was carried out to find out the compatibility between the drug and the polymer. About 1 mg of drug and 100 mg of KBr were taken in a mortar and triturated. A small amount of the triturated sample was taken into the DRS sample holder and scanned from 4000 cm^{-1} to 400 cm^{-1}at resolution of 4 cm^{-1} and 15 scans per spectrum.

3.2 Differential scanning calorimetry (DSC)

This was carried on drug loaded microspheres using a differential scanning calorimeter (Mettler Toledo, USA). For this, the powder sample (1 to 5 mg) was packed in an aluminum DSC pan. An aluminum lid was placed on the top of the pan and was crimped. The crimped pan was placed in the sample cell along with an empty pan as a reference. Temperature was increased to 300 ^oC from 0^oC at a rate of 10^oC /min. The thermal cell was purged with dry nitrogen at 20 mL/min (Chatwal et al., 2012).

3.3 Olfactory analysis of trial batches.

The panel of four people is selected. The peoples who are selected, their nose is quite sensitive to particular odor or who are expert in that field. The samples of trial bathes are weighed in the equal quantities and placed into the Petri-dishes.

Each Petri-dish is covered with its leads. This has done into the clean room where there is no any other odor or smell. Each person in the panel has allowed taking the odor. After each sample the coffee beans are there to refresh the nose to get better results. The marking has given according to persons own experience (0 to 10 scale).

The mean values of each sample is recorded and tabulated. The graph has plotted for Trial No. Vs Odor score (mean).

Table no. 2: Reference Olfactory Score.

Sr. No.	Olfactory Score	Type of Odour
1	0 to 03	Intensive
2	03 to 05	Foul
3	05 to 07	Good/Acceptable
4	07 to 10	Pleasant

3.4 Stability study

The study consists of selected formulations were kept in environmental stability chamber maintained at 40 ºC ± 2 ºC/75% ± 5%RH for 30 days and then samples were analyzed for physical appearance, odor marking at 10, 20, 30 days (Gad, 2008).

4. Results and Discussions

4.1 Drug-polymer compatibility study by FT-IR spectrophotometer

FT-IR spectroscopy study was carried out separately to check the compatibility of the drug and polymer used for the preparation of microspheres. FT-IR was performed for the drug, polymer and physical mixture of drug and polymer. The spectrum obtained from FT-IR spectroscopy studies at wavelength from 4000 cm^{-1} to 400 cm^{-1} are shown in figure 1, 2 and 3 and the characteristic peaks obtained are shown in table 1, 2 and 3.

Fig no 1: IR Spectra of API.

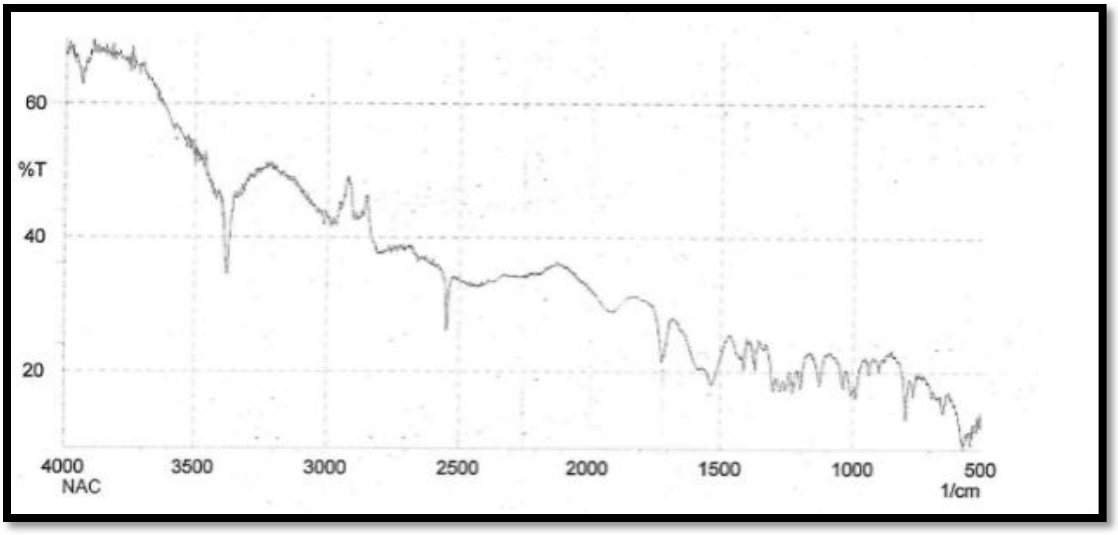


Fig no 2: IR Spectra of polymer.

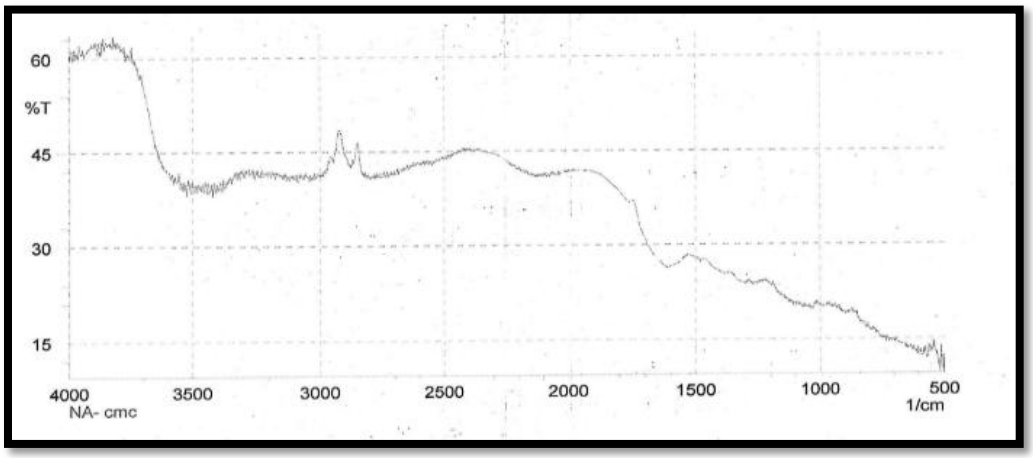


Fig no 3: IR Spectra of Physical mixture.

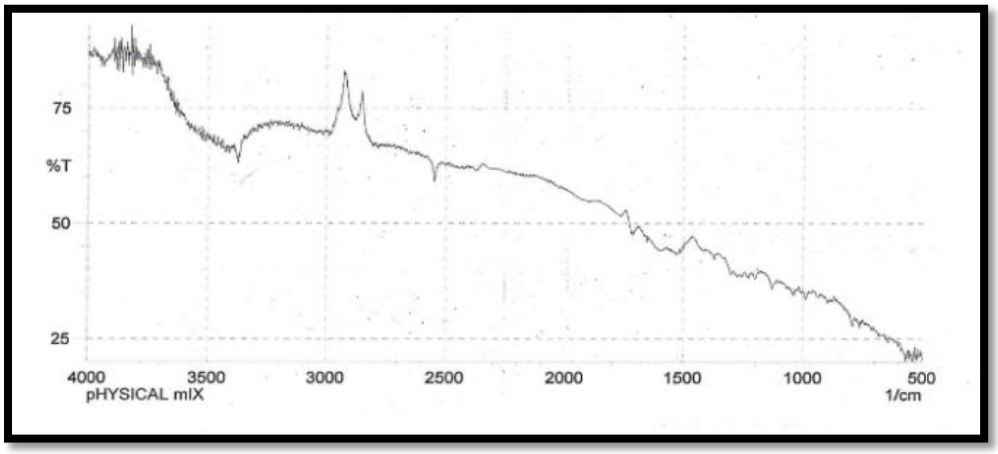


Fig no 4: Overlapping IR Spectra of physical mixture and API.

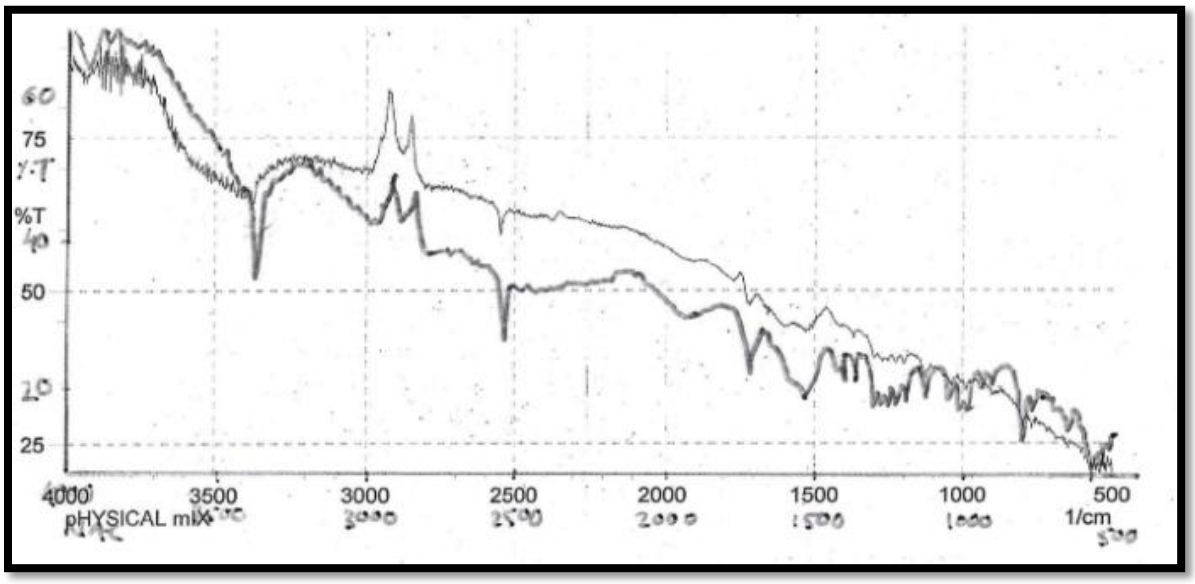


Table no 3: IR interpretation of API.

Obtained peak value (cm^{-1})	**Standard ranges of wave number (cm^{-1})**	**Bond**	**Characteristic functional group**
3342.42	3400-3250	N-H(stretching)	Amine
1677.22	1760-1690	C = O(acid)	Alcohols, esters, carboxylic acid
930.11	950-910	O = H (Bending)	Alcohol
1650	1600-1700	C –H (Streching)	Alkane
2552.33	2563-2522	S = H(stretch)	Sulfur
1050	800-1200	C-C(Streching)	Aromatic

Table no 4: IR interpretation of Physical mixture.

Obtained peak value (cm^{-1})	**Standard ranges of wave number (cm^{-1})**	**Bond**	**Characteristic functional group**
3351.32	3400-3250	N-H(stretching)	Amine
1679.42	1760-1690	C = O(acid)	Alcohols, esters, carboxylic acid
930.11	950-910	O = H (Bending)	Alcohol
1650	1600-1700	C –H (Streching)	Alkane
2555.74	2563-2522	S = H(stretch)	Sulfur
1052.43	800-1200	C-C(Streching)	Aromatic

4.2 Differential scanning calorimeter (DSC)

This was carried out to find out possible interaction between the drug and polymer. The thermograms obtained from differential scanning calorimeter of pure drug, Na-CMC and drug loaded finalized formulation was shown in figure 25, 26 and 27.

Fig No 5: DSC thermogram of pure drug.

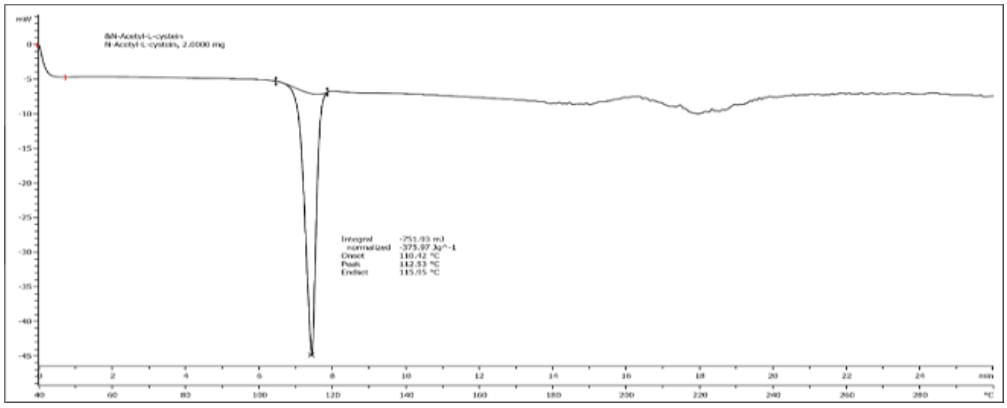


Fig No 6: DSC thermogram of Na-CMC

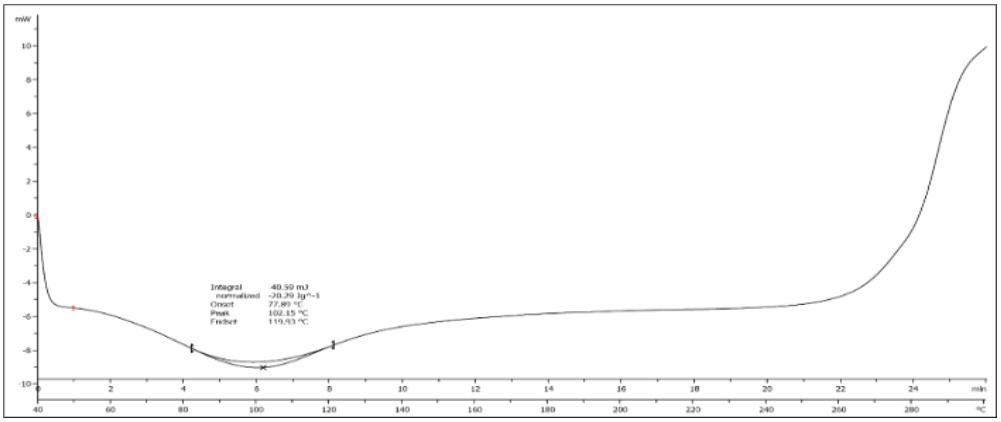
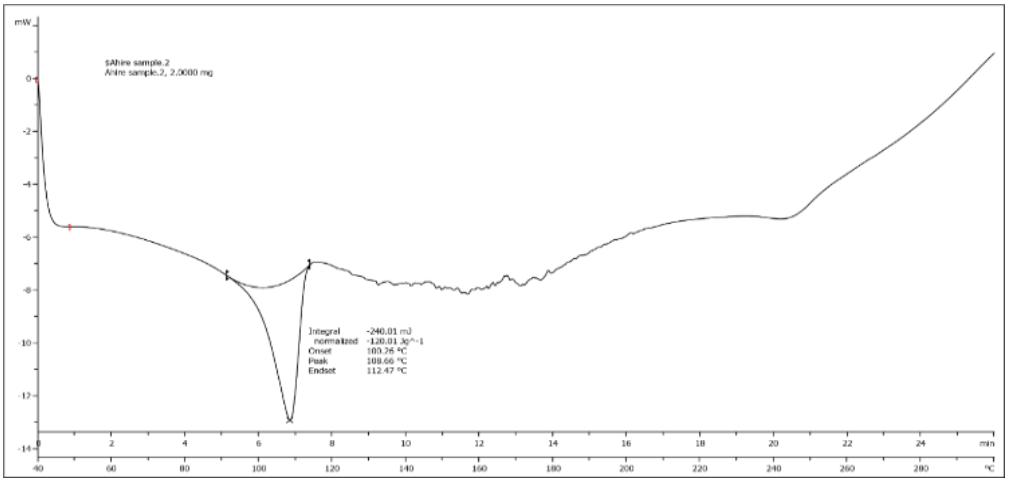


Fig No 7: DSC thermogram of drug loaded finalized formulation.



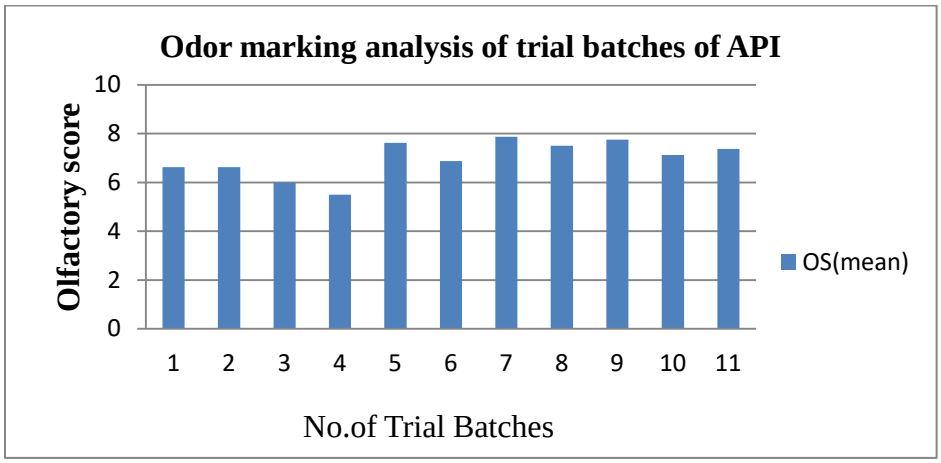
DSC thermogram of API shows a sharp endothermic peak at 112.53^{o}C andof Na-CMC at 102.15 ^{0}C. The thermogram of the drug loaded finalized formulation also shows peak at 108.66 ^{o}C. This DSC study further confirms that there was no drug-polymer interaction in formulations.

4.3 Olfactory analysis of trial batches.

Table no. 5: Olfactory score and its mean values of trial batches of NPS.

Trial no.	Panel of four people(OS)				
	A	**B**	**C**	**D**	**Mean**
1	5.5	6.5	7	7.5	6.62
2	7.5	5.5	7	6.5	6.62
3	8	6	7.5	6.5	7
4	5	4.5	6	6.5	5.5
5	8	8.5	7.5	6.5	7.62
6	7	7.5	6.5	6.5	6.87
7	7.5	7.5	8.5	8	7.87
8	8	8	7.5	6.5	7.5
9	6.5	8.5	8.5	7.5	7.75
10	7.5	8.5	5.5	7	7.12
11	8.5	7.5	7	6.5	7.37

Fig no 8: Odor marking analysis of trial batches.



The odor marking analysis of trial batches shows that in trial no.7 there is maximum masking of odor and the average value is 7.87.

4.4 Stability study

Table no. 6: Stability observations in 30 days

Evaluation parameters	**Initial**	**10**	**20**	**30**
Physical appearance	white colour	white colour	white colour	white colour
Odor marking	7.77	7.75	7.47	7.35

The results of effect of temperature and humidity at 40 ºC ± 2 ºC/75% ± 5%RH for 30 days in environmental stability chamber on selected formulation are shown in table. There was no significant change in their physical appearance, of the samples analyzed after 10, 20 and 30 days of storage & were similar as initial and there was no significant change in odor marking after 1 month. Hence, from the above results, it can be concluded that the developed formulations were stable and retained their pharmaceutical properties over a period of 1 month.

5. Conclusion

In the present study, attempts were made to study the olfactory properties of the substance. From the olfactory analysis it is concluded that, the amino acids have objectionable odor and these are also having nutritional value. The possible drug and polymer interaction during the time of preparation was studied using FT-IR and DSC analysis. The result of FT-IR study revealed that there was no interaction between the selected drug and polymer and result of DSC showed that the stability of drug was not affected by the procedure used for the formulation of the coated NPS. The odor marking analysis were also done for the finalized batch and found to be having good masking ability of the polymer. The final formulation was studied for effect of temperature and humidity in stability chamber for 1 month. The studies indicated that the formulations were stable and retained their pharmaceutical properties over period of 1 month.

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Corresponding Author:

S. P. Ahire[1]*,

[1]School of Pharmaceutical Sciences, Sandip University, Nashik, Maharashtra.

Email: shubhamahire7@gmail.com