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Isolation, Recovery and Analysis of Active Drug From Formulation

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ABSTRACT

Drugs are used in pharmaceutical formulation to serve the mankind and help them to maintain their Quality of Life. As per literature survey we found that there are a fair number of paper that explains the formulation of dosage form by certain drugs, but none of them with explaining the aspect of isolation and retrieving of the active drug from the dosage form. In the current study Paracetamol is taken as the active drug which is used to formulate the best batch of tablet and then the drug is retrieved back from the best found formulation by the help of specific solvent. This solvent was determined by trial of several combinations and the best selected results are mentioned. 96.24 % of the active agents were isolated by the help of selected solvent. The drug compatibility study was carried out by Fourier Transform Infrared spectroscopy (FT-IR) and the structure determination of the isolated active agent was carried out by the Nuclear Magnetic Resonance (NMR) results. The assay of isolated active agent was carried out by UV spectroscopy. All these analytical data helped to elucidate the structure of isolated active agent and was found similar to that of Paracetamol.

Keywords: Quality of Life, active agent, paracetamol, UV, FT-IR, NMR.

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INTRODUCTION

The oral route is the most popular and traditionally used route of taking medication. Despite of having some disadvantages like slow absorption still date it is the most preferred route of drug delivery[1]. Paracetamol is chemically N-(4-hydroxyphenyl)-acetamide. The main mechanism of action proposed is the inhibition of cyclooxygenase (COX), and recent findings suggest that it is highly selective for COX-2. Because of its selectivity for COX-2 it does not significantly inhibit the production of the pro-clotting thromboxanes.While it has analgesic and antipyretic properties comparable to those of aspirin or other NSAIDs. It is official in Indian Pharmacopoeia, British Pharmacopoeia and United States Pharmacopoeia. According to literature survey there many papers that reveal formulation and evaluation parameters of paracetamol tablets, but there are no literature available for isolation and evaluation of active drug from the tablet dosage form[a].

MATERIALS AND METHOD

Paracetamol was obtained from VAMA PHARMA (Nagpur, India). Other ingredients used were of analytical grade. All the tests were performed at Priyadarshini J.L. College of Pharmacy (Nagpur, India).

FORMULATION OF TABLET

Drug-Excipients Compatibility Study by FTIR [b]

Fourier-transform infrared **(**FT-IR) spectra were obtained using an FT-IR spectrophotometer. The Paracetamol and Excipients were previously ground and mixed thoroughly with potassium bromide, an infrared transparent matrix, at 1:5 (Sample: KBr) ratio, respectively. The KBr discs were prepared by compressing the powders at a pressure of 5 tons for 5 min in a hydraulic press (Press Pellet Technique Method). Forty scans were obtained at a resolution of 4 cm-1, from 4000 to 400 cm^{-1}.

Preparation of tablets [c]

Four different batches of tablet were prepared using wet granulation technique. The composition of single tablet per batch is given in table 1. Calculated amount which was required to prepare 600 mg paracetamol tablets containing 500 mg drug, binder and filler was mixed uniformly. A sufficient amount of granulating agent (water) was added slowly to prepare wet mass. Granules were prepared by sieving method using 20# sieve. Further, granules were dried at 35-45ºC for six hours. The dried granules were stored in desiccators until compression of tablets. Prior to compression the dried granules were subjected to micromeritic study and evaluated for their flow characteristics and lubricated granule were analyzed for the potency studies. The required amounts

of granules were weighed and compressed using 18 mm flat faced punch diameter. The compressed tablets of each batch were stored in air tight container at room temperature for further study. Such method of tablet production has previously been described by several authors who provided reproducible experimental results in terms of in-vitro release. Different batches were prepared and separately analyzed and the tablets with best results were further taken for isolation of active ingredients.

Table 1: Composition of Batches F1-F4 by using different excipients (%)

S. No.	Composition	F1	F2	F3	F4
1	Paracetamol	83.33	83.33	83.33	83.33
2	Maize Starch	14.42	16.067	16.279	15.25
3	Magnesium Stearate	0.25	0.25	0.221	0.25
4	Potassium Sorbate	0.10	0.10	0.0833	0.10
5	Talc	-	0.167	-	-
6	Aerosil	0.167	0.0833	0.0833	0.167
7	Sodium Metabisulphite	0.067	-	-	0.067
8	PVPK – 30	-	-	-	0.833
9	Maltodextrin	1.67	-	-	-

Evaluation of granules:

Granules were evaluated for all pre-compression parameters like angle of repose, bulk density, tapped density, bulkiness, hausner's ratio and compressibility index. The evaluation was done using all the methods as per specified in Indian Pharmacopoeia.

Evaluation of Tablets

All set of tests specified in the official monograph were performed and results were tabulated.

Weight variation:

All prepared tablets were evaluated for weight variation as per Indian Pharmacopoeia monograph. Twenty tablets of each batch were used to evaluate weight variation among tablets and mean and standard deviation was calculated.

Friability:

Tablets of all batches were used to evaluate friability as per Indian Pharmacopoeia monograph. Friability testing was done by Rooche's Friabilator with readings in triplicate.

Hardness:

Hardness of all batches was determined using Monsanto hardness tester. The test was carried out in triplicate for all batches as per Indian Pharmacopoeia monograph for uncoated tablets.

Thickness:

The thickness of the matrix tablets was determined using vernier caliper and the results were expressed as mean values of 10 determinations, with standard deviations.

Drug content:

The tablets were powdered, and 250 mg equivalent weight of Paracetamol in tablet powder was accurately weighted and transferred into a 100 ml volumetric flask. Initially, 10 ml of phosphate buffer (pH 7.4) was added and shaken for 10 min. Thereafter, the volume was made up to 100 ml with buffer. Subsequently, the solution in volumetric flask was filtered, and 1 ml of the filtrate was diluted and analyzed at 247 nm using UV-visible spectrophotometer (Shimadzu UV-1700, Japan).The drug content of the each sample was estimated from their previously prepared standard curve.

***In-vitro* drug release study:**

In-vitro drug release was studied using Electrolab Dissolution Apparatus, in 900 ml phosphate buffer pH 7.4, maintained at 37±1°C for 4 h, at 100 rpm. 5ml of sample was withdrawn after specified time interval, and was replaced by an equal volume of fresh dissolution medium. Collected samples were analyzed spectrophotometrically at measured wavelength of 247 nm, and cumulative percent drug release was calculated. The test was performed in triplicate to assure significance of results. Drug release profile was studied using percentage drug release Vs time (h) plot.

Isolation of active agents from the tablet dosage form

Preparation of Solvent Solution:-

The solvent was prepared by mixing methanol, chloroform and water. The ratios of individual solvents were optimized and tabulated.

Isolation Procedure

Twenty tablets were crushed uniformly and the powder was transferred to volumetric flask. A fair amount of prepared solvent was added and the flask was placed on the magnetic stirrer for 30 minutes. Then solution was centrifuged at 3000 rpm for 5 minute and supernatant was transferred to beaker and covered with glass lid with slight opening at one corner. The beaker was allowed to stand overnight. The lid was scratched and crystals were recrystallized with methanol and Percentage recovery was calculated using following formula on dry weight basis:-

$$\% \text{ Recovery} = \frac{\text{Amount of drug recovered(in Kg)}}{\text{Amount of Drug in 20 tablets (in Kg)}}\ x\ 100$$

Analysis of Isolated active drug

The lid was scratched and recovered drug were analyzed using UV-Visible spectrophotometer, Fourier Transform Infrared (FT-IR) spectrophotometer and Nuclear Magnetic Resonance (NMR) spectrometer.

RESULTS AND DISCUSSION

Interpretation of FTIR spectra

Compatibility studies were performed using FTIR spectrophotometer. The characteristic absorption peaks of pure drug and mixture with other excipients were obtained at different wave numbers. The peaks obtained in the spectra of pure drug correlates with the peaks of drug with other excipients. It does not show any major changes in peaks which indicate no well-defined interaction in drug and excipients spectrum. This indicates that the drug is compatible with the formulation components. The spectrum for pure drug and excipients are shown in figure 1& 2 and interpretations of spectrum are reported in table 1.

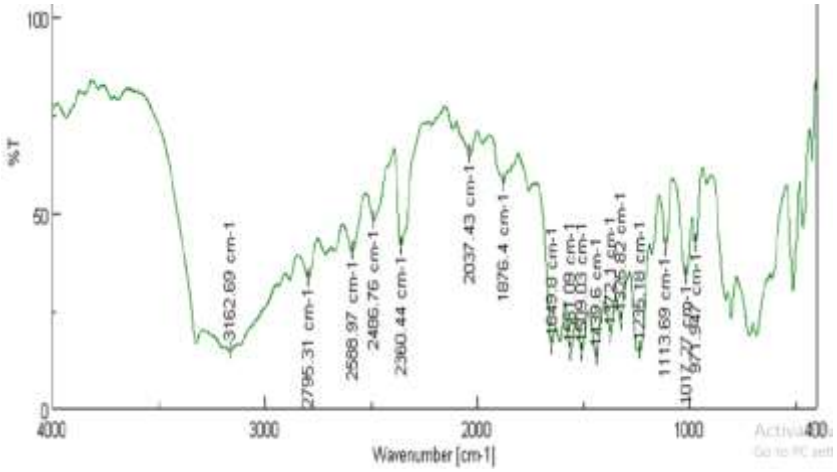

Figure 1:FT-IR of Paracetamol

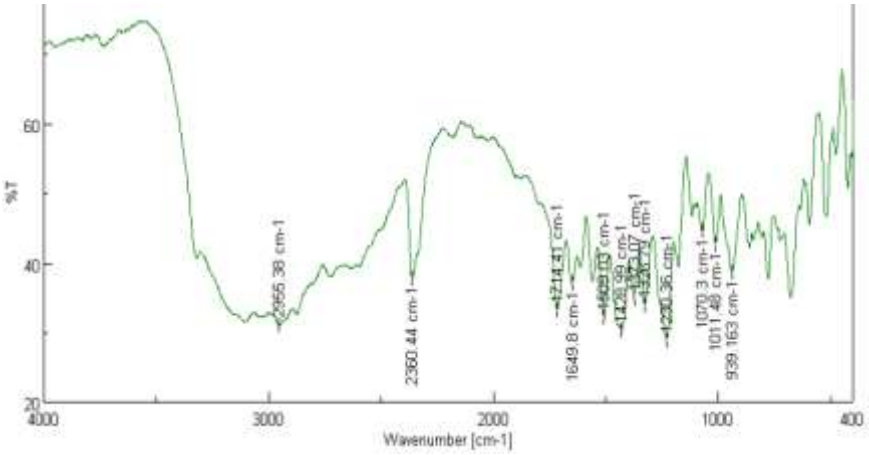

Figure 2:FT-IR of Paracetamol along with all excipients

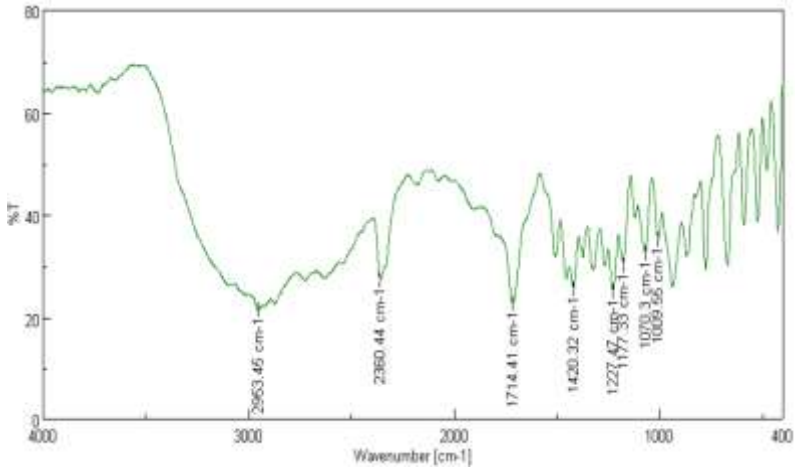

Figure 3: FT-IR of isolated active drug from tablet dosage form

Table 1: Interpretation of FT-IR Spectra

S.No.	Group	Wave number (cm^{-1})		
		Paracetamol	Paracetamol along with all excipients	Isolated Active Drug
1	CH3 asymmetrical stretching	3162.69	2955.38	2953.45
2	O-H…O stretching combination	2360.44	2360.44	2360.44
3	C=O stretching	1714.41	1714.41	1714.41
4	Amide II band	1509.03	1509.03	1508.73
5	CH-CO deformation	1420.32	1428.99	1420.32
6	OH in plane deformation	1325.82	1326.79	1326.05
7	C….C stretching	1227.47	1230.36	1227.47
8	C-N-H group	1070.30	1070.30	1070.30
9	Para-substituted aromatic ring	1009.55	1011.48	1009.55

Evaluation of granules

The various micromeritic characteristics and flow properties of the granules obtained by wet granulation for each batch and reference batch did not show any significant variation in their values. The values of physical properties of all batches are shown in table 2 having average of triplicate readings, with standard deviation (table 2).

Table 2: Micromeritic characteristics and flow properties of the granules

S. No.	Properties	Formulations			
		Batch F1	Batch F2	Batch F3	Batch F4
1	Bulk density (g/cm^3)	0.376(±0.017)	0.404(0.021)	0.436(0.025)	0.424 (0.032)
2	Tapped density (g/cm^3)	0.427(±0.022)	0.434(0.019)	0.456(0.025)	0.430 (0.033)
3	Bulkiness (g/cm^3)	2.66(0.031)	2.48(0.024)	2.29(0.029)	2.36(0.025)
4	Carr's index	11.857(0.31)	8.415(0.37)	4.40(0.33)	14.0(0.36)
5	Hausner's ratio	1.130(0.30)	1.074(0.32)	1.046(0.26)	1.014(0.24)
6	Angle of repose (degrees)	28.37(0.028)	27.73(0.022)	21.49(0.021)	22.57(0.025)

Evaluation of Tablets [d]

The tablets from each batch were evaluated for several parameters and compared with standard Crocin™. The values were tabulated in form of average of the triplicate readings (table 3). The results of batch F4 was found to be best and tablets of batch 4 were further used for release pattern studies. The results of drug release are shown in figure 4.

Table 3: Evaluation of tablets

S. No.	Batch	Evaluation tests			
		Hardness (Kg/cm^2)	Friability (%)	Assay (%)	Drug Release (%)
1	F1	5.5	0.5	96.54	85
2	F2	5.0	0.8	96.82	87
3	F3	4.5	0.4	97.24	93.42
4	F4	6	0.3	99.98	95.67
5	Std.(Crocin)	6	0.29	99.90	95.50

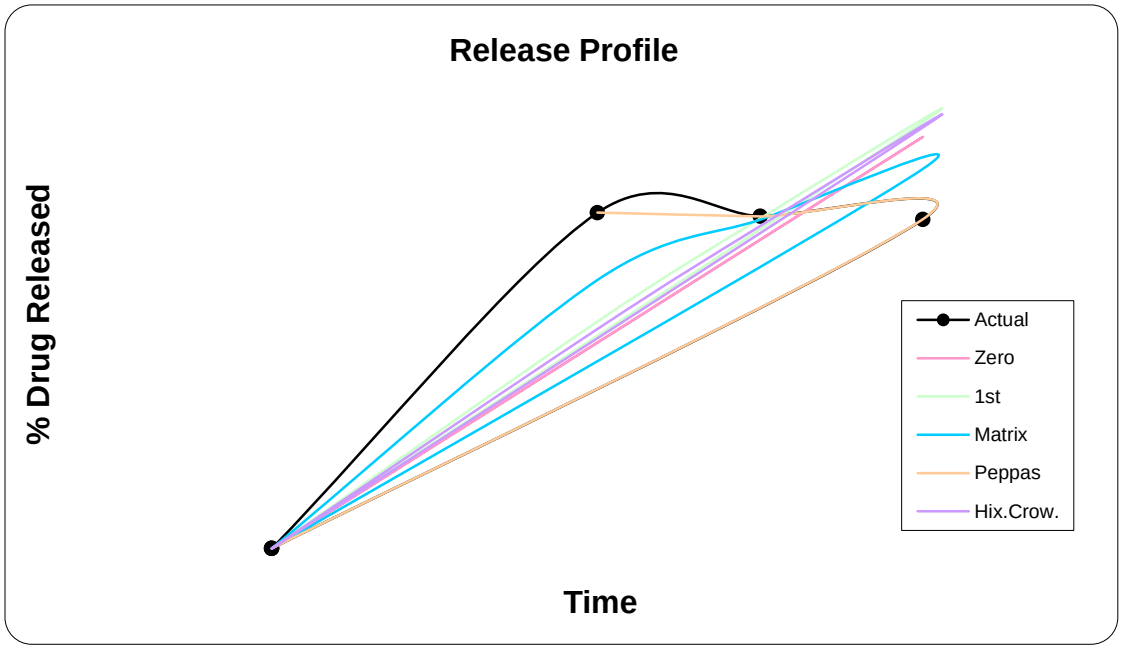

Figure 4:Drug release pattern F4 batch

Results of Isolation of active agents from the tablet dosage form

The active agents were recovered by the extraction procedure. Different set of solvents were used and the % recovery of the active agents were tabulated. Further analytical studies were carried out to confirm the structure of the recovered active agents. The results of UV analysis and NMR spectroscopy are shown in figure 5, 6 and figure 7 respectively.

Table 4: Isolation of active agents.

S. No.	Batch	Ratio of solvents used (Methanol : Chloroform : Water)	Drug Recovered (%)
1.	F4	6 : 3 : 1	75.89

2.	6 : 2 : 2	68.28
3.	6 : 3.5 : 0.5	64.28
4.	6 : 4 : 0	48.69
5.	5 : 4 : 1	93.54
6.	5 : 5 : 0	47.51
7.	5 : 3 : 2	58.24
8.	5 : 2 : 3	84.58
9.	4 : 4 : 2	59.64
10.	4 : 3 : 3	56.23
11.	4 : 3.5 : 2.5	68.58
12.	4 : 5 : 1	96.24

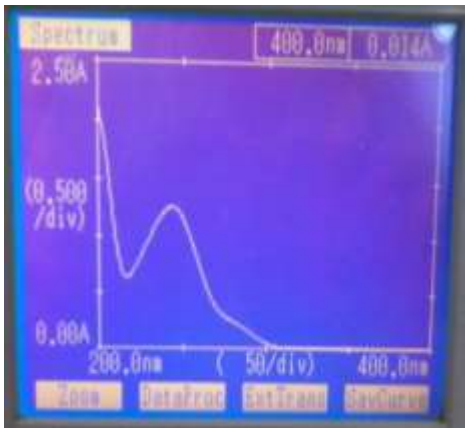

Figure 5:- UV spectra of recovered active agent

Figure 6:- λ max of recovered active agent

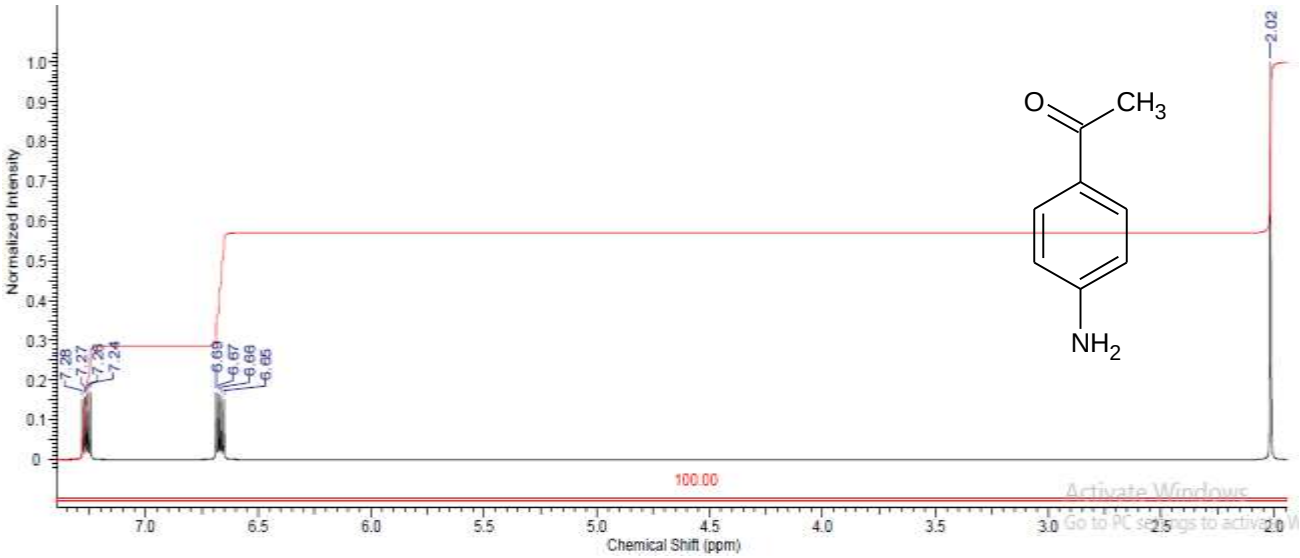

Figure 6: NMR spectrum of recovered active agent

CONCLUSION

Formulation of the best possible batch was carried out using mentioned excipients. The entire evaluation test was carried out and batch 4 was selected as the best one. Samples tablets from this batch were used for the isolation studies of active agents. The solvents that showed best isolation

of the active agent was Methanol: Chloroform: Water in the ratios of 4:5:1. Analytical results of FT-IR, UV, and NMR helped to elucidate the structure of the recovered active agents which was found similar to that of paracetamol.

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