Available online on 15 Dec, 2022 at http://www.hjhs.co.in/index.php/hjhs

Himalayan Journal of Health Sciences

Published by Himalayan Group of Professional Institutions
Associated with Himalayan Institute of Pharmacy

Research Article

Open Access

Formulation and Evaluation of Itraconazole Nanocapsules

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Abstract

An objective of a present research has been able to prepare as well as analyze Itraconazole Nanocapsules through using emulsion solvent evaporation method. Itraconazole has been overfilled of ethyl cellulose & hydroxypropyl methylcellulose Nanocapsules and that was able to prepare through emulsion solvent evaporation technique. The outcomes like Fourier transform infrared implied a steady identity like Itraconazole Nanocapsules filled as for ethyl cellulose Nanocapsules and then also absence like drug - excipient interplay. Compatibility research findings like FTIR & differential scanning have been used to start investigating that there's no incompatability inside the composition. A morphometric size of the particles like Itraconazole Nanocapsules has been done through SEM. Nanocapsules has been analyzed such as total composition codes has been f1 to f8. A % yield has been obtained to be 73.22% to 88.91%. Drug content has been 65.9 to 98.4%. A size of the particles like Nanocapsules 80 µm to 22 µm, drug entrapment efficiency has been 54.3% to 91.3 %, a drug loading capabilities has been 97.8% to 56.9%. A swellability studies has been 0.6 sec to 1.6 sec. in vitro dissolution studies like best formulation f8 has been did find of being 61.78%. An In-vitro drug dissolution obtained data has been equipped to numerous mathematical equations such like zero order, 1st order, higuchi matrix & korsmeyer peppas model. Itraconazole Nanocapsules continues to follow model having r2 value has been 0.937, 0.399, 0.899, 0.785 & m value has been 1593, 0.061, 11409, 2.560. The discharge of drug out from Nanocapsules increased up of about 45 mints. Itraconazole loaded as for ethyl cellulose & HPMC Nanocapsules have been able to prepare below optimum condition and it display great discharge characteristic features.

Keywords: Itraconazole, Nanocapsules, In-vitro dissolution studies, FTIR & DSC

Article Info: Received 22 Nov 2022; Review Completed 13 Dec. 2022; Accepted 15 Dec. 2022

Cite this article as:
Dudekula A, Challa M, Mutcherla PK. Formulation and Evaluation of Itraconazole Nanocapsules. Himalayan J H Sci [Internet]. 2022 Dec 15 [cited 2022 Dec 15]; 7(4):33-41. Available from: http://www.hjhs.co.in/index.php/hjhs/article/view/158

DOI: 10.22270/hjhs.v7i4.158
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1. Introduction

Nanocapsules have been constituted like synthetic polymer membrane structure as well as center like oi, where it encapsulates opioids that could dispersed out and under controlled circumstances, through responses to environmental, chemical, thermoelectric, as well as physiological provokes. (1) Nanocapsules were also colloidal as well as synthetic through inter-facial accumulation did perform polymeric materials (PLA, PLGA, PCL, and PEG). This is appropriate for such distribution like hydrophobic opioids. Liposomes nanocapsules are often used for multi-drug-resistant case scenarios through rodent melanoma. For a assembly of a multi-layer shell, connections such like electrostatic force, covalent bonding, hydrogen-bonded, etc. Dissociation of a sacrificial template leading to formation of a porous caplets. Nanocapsules have been corresponding to one vesicular system that integrates a opioid within its cavity, where it comprised like fluid core but rather matric materials encircled through polymeric membrane. (2) A aperture encapsulates an active ingredients with in liquid form but rather solid like a single-molecule diffusion. Those certain porous nanocapsules have enough capabilities of about incorporate a wide range of materials such like colorants, opioids, metal-catalyzed, but also biodegradable polymers like protein molecules as well as nucleotide bases. (3)

Nanocapsules, which also are sub-micron through surface area, while given intravenously, achieve towards the goal but also discharge a entrapped drug. Nanocapsules, where it start measuring 1 thousandth of such a mm, could be absolutely covered with such an autoantibodies upon that area, where it supports through trying to direct those out from circulatory system to such an caused melanoma. (4)

After trying to reach towards the melanoma, a kind immediate blow takes place and it tends to make caplets of about start opening but also outflow with their therapeutic components. Upon that area of a polymer, there's several relatively small gold particulate within range like 6 nanometers i.e. 6 million of such a mm

where it adhere across it and have been specialized to a laser beam as well as lead a caplets of about posture of their opioid capacity just at requested time. (5)

Polymeric nanoparticles made of natural but rather synthetic fibers have been simple to change peripherally but also have been, through general, consistent, their own characteristics could be synchronized to accomplish improved bioactivity or a controlled release drug delivery through specific places. Biopolymers have now been broadly used during the preparedness like system is used to control release of drug. (6) Which could also stay stable definite fragile particles, such like protein molecules, polypeptide, and genetic material, and it can be used such as site-specific opioid attacking. Preparedness like degradable nanoparticles such as implementation through tissue engineered is indeed sought. Since they are bio-based, they could persist such as days or weeks as well as discharge a opioid with in attack throughout that period. PLA as well as PLGA have demonstrated to be successful as for subcellular opioids. (7) PLGA is typically merged with PEG, just like PEGylation tends to increase solubilization as well as stabilization through liquid, lessens intra-molecular agglomeration, significantly reduces humoral immunity, as well as enhances its universality of a opioid with in circulatory system. (8)

2. Materials and Methods

Itraconazole (Hetero drugs Limited), Ethylcellulose (Rohm Gmbh & CoKG, Germany), HPMC (SD Fine Chemical Limited), Ethanol (Ruchi Global limited, Madhya Pradesh).

Compatibility studies:

IR studies: In a preparedness of opiid as well as polymer could communicate with one another, this leads to a instability like opioid pre-formulation research regarding a opioid but also polymer interplay. (9) They're really quite crucial through relevant polymer. FT-IR spectroscopy has been employed to determine connectivity among itraconazole as well as the cellulose polymer (Perkin Elmer Jasco FTIR- 401, Japan).

Differential scanning calorimetry: The output of such a DSC is just a plot of heat flux (rate) v/s temp at such a standard temp frequency. It gives the content most of physical properties of a specimen. It is in crystalline rather than amorphous in environment. In formulations it illustrates complex interconnections between both the opioid and also polymer matrix, as per the thermograms. (10)

Morphology of the particles

A subsequent methodologies are being used to ascertain a size of the particles, particle size, but also morphology characteristics of a Nanocapsules.

Scanning Electron Microscopy

Scanning Electron Microscope is a technique (SEM). This is very beneficial such as ascertaining the general structure as well as morphology characteristics of Nanocapsules. A morphology characteristics as well as surface profile of the both encased Nanocapsules as well as Ethyl cellulose Nanocapsule have been did find through Scanning Electron Microscopy. (11) A particulate have been frozen, but also absolutely covered with gold palladium to accomplish a film like 20nm width (Sputter coater, Balzers SCD 004, Liechtenstein) but also recognized microscopic examination (SEM, JSM-6400, Tokyo, Japan).

Procedure of Itraconazole Nanocapsules

The Itraconazole Nanocapsules have been acquired even by emulsion solvent evaporation technique through using deionised water as such an exterior process. The interior phase comprises of such a great solutes ethyl which include Itraconazole as for concentration like polymeric materials such as HPMC& Ethyl cellulose. (12) A opioid as well as polymer matrices seem to be co-dissolved in an organic phase mix to polymer matrices as for various ratios. A opioid solution has been gently infused through use of injector this into the exterior liquid state below stirring. A process has been agitated about as 800 revolutions per minute consistently for around 1 hr. Incuding the pleasant solutes trying to defuse more into the poor solute. Particles progressively hardened and created Nanocapsules. A process has been filtrated of about totally separate it Nanocapsules from a preparatory process. A resulting material has been cleaned as for purified water and left to dry. A whole procedure was conducted out over room temp. The ratio for drug& polymers were showed. (13)

Table 1. Formulations of Itraconazole Nanocapsules

S.No.	Ingredients	F1	F 2	F 3	F 4	F 5	F6	F 7	F 8
1	Itraconazole	1.5	2.5	1.5	2.5	1.5	2.5	1.5	2.5
2	Ethyl Cellulose	0.5	1.0	1.5	2.0	0.5	1.0	1.5	2.0
3	HPMC	1.0	1.5	1.0	1.5	1.0	1.5	1.0	1.5
4	Ethanol	15 ml	15 ml	15 ml	15 ml	15 ml	15 ml	15 ml	15 ml
5	Distilled water	100 ml	100 ml	100 ml	100 ml	100 ml	100 ml	100 ml	100 ml

Evaluation of Nanocapsules:

Percentage production yield (PY)

$$PY\ (\%) = \frac{\text{Practical mass of Nanocapsules}}{\text{Practical mass of Nanocapsules}} \times 100$$

Theoretical mass

Each composition has been an outcome of triplicates as well as a PY (%) has been Measured.

Entrapment efficiency: A Nanocapsules has been able to prepare through Emulsion solvent evaporation method. This was subjected to centrifugation there as 14,000 revolutions per minute such as 40 min there as 10°C. A quantity like Itraconazole has been encased

through into Ethyl cellulose & HPMC. This was the differentiation among total quantitites which are used to organize Nanocapsules and then the quantity has been present in a culture medium. The quantity like unlimited Itraconazole within a culture medium has been evaluated through UV-spectrophotometer there as 262 nanometers. (14) This is measured even by following formulae

$$\%EE = \left\{ \frac{M_{\text{Initial drug}} - M_{\text{Free drug}}}{M_{\text{Initial drug}}} \right\} X100$$

Where

"$M_{\text{Initial drug}}$" is the mass of initial drug used for the assay

"$M_{\text{Free drug}}$" has been the mass of free drug identified with in culture medium ever since emulsification of a aqueous suspension.

Drug loading efficiency: Drug encapsulation effectiveness has been eliminated as well as the leftover sediment cores (precipitations) have been thoroughly cleaned through deionised water. It's also diffused inside a mix like Chloroform: acetonitrile (2.5:2.5, v/v) inside a 10 mL beaker and used to make sure the entire harvesting like opioid through the Nanocapsules, then that has been ultrasonicated untill 30 min. (15) A quantity has been created of about 10ml with chloroform. A standard solution has been subjected to centrifugation about as 14,000 revolutions per minute about as 10°C untill 30 min but also supernatants have been acquired as well as reviewed through triplicate again for overfilled opioid through UV spectrophotometer at 262nm.

Particle size determination: Size of the particles of Nanocapsules has been ascertained via using the electron microscopy process. Approximately 100 Nanocapsules have been taken into account as a size of the particles. A allocation of size of the particles has been assessed through going to suspend through hydrate. (16)

Equilibrium swelling studies of Nanocapsules: A preweighed quantity Nanocapsules has been positioned through Phosphate-buffered (pH 7.4). This is permitted of abut swell at such a steady weight. A Nanocapsules have been eliminated as well as blotted as for filter paper, but also about their alters through weight have been assessed. A degree of swelling (a) has been determined by calculating even by given equations. (17)

α=wg-wo/wo

Where

Wo is the initial weight of the Nanocapsules and

Wg is the weight of the Nanocapsules at equilibrium swelling in the medium.

Drug content determination: 50mg of Itraconazole Nanocapsules has been smashed as well as suspended in a liquid of about extricate a opioid as from Nanocapsules. Now since 24 h, a filtration has been assessed UV- visible spectrophotometer there as 262 nanometers such as drug content on that hydrate just like blank. (18)

***In-vitro* drug release studies:**

In-vitro drug release studies were conducted out using USP XXIV dissolution equipment type II, with 500 ml of dissolution medium. This is retained at 37±0.5 °C such as 45 Mits, there as 50 revolutions per minute, but also pH 7.4 ± 0.2 phosphate buffer like dissolution medium. (19) Outcomes like *In-vitro* release profile acquired for all of preparations have been obtained by plotting through configurations of data treatment as follows:

- Log cumulative percentage drug remaining V/S a time (first order kinetic model)
- Cumulative percentage release of drug V/S square root of time (Higuchi model)
- Cumulative percent drug remaining V/S the time (zero order kinetic model)
- Log cumulative Percent Drug released versus log time (korsmeyer's peppas model)

Data Analysis: To analyse a method for the discharge but also release rate kinetic model of a dosage form, the information acquired and it has been equipped into the Zero order, 1st order, Higuchi matrix as well as Korsmeyer but also Peppas model. (20-22) Contrasting a r-values are acquired, a best-fit concept has been chosen.

Zero order kinetics: Drug dissolution through the pharmaceutical dosage forms does not disaggregate and a opioid will be released gently, presuming that such region doesn't really alter and also no equilibrium state have been acquired. It can be given by the following equation:

$$Q_t = Q_o + K_o t$$

First order kinetics: To review a 1st order release rate kinetics its release rate data have been equipped towards the following formula.

$$\text{Log } Q_t = \log Q_o + K_1 t / 2.303$$

Higuchi model: This model is established by numerous theoretical concepts. To review the discharge of water-soluble as well as low soluble opioids.They are integrated in to semisolids or even solid matrices, an equation has been

$$Q_t = K_H . t^{1/2}$$

Korsmeyer and Peppas release model:

To review such a concept a release rate data have been fitted towards the following formula

$$M_t / M_\infty = K.t^n$$

n is the Diffusion exponent for release of drug which is depending on the shape of the matrix dosage form.

3. Results and Discussion:

Compatibility studies

IR studies

A IR spectrum of a pure Itraconazole specimen has been documented through Fourier Transform Infrared. This would be compared to standard functional group frequency range Itraconazole as such seen in Table 2. FTIR spectrum like composition as seen in Figure 1.

COMPARISON OF FT-IR SPECTRA OF ITRACONAZOLE AND FORMULAE

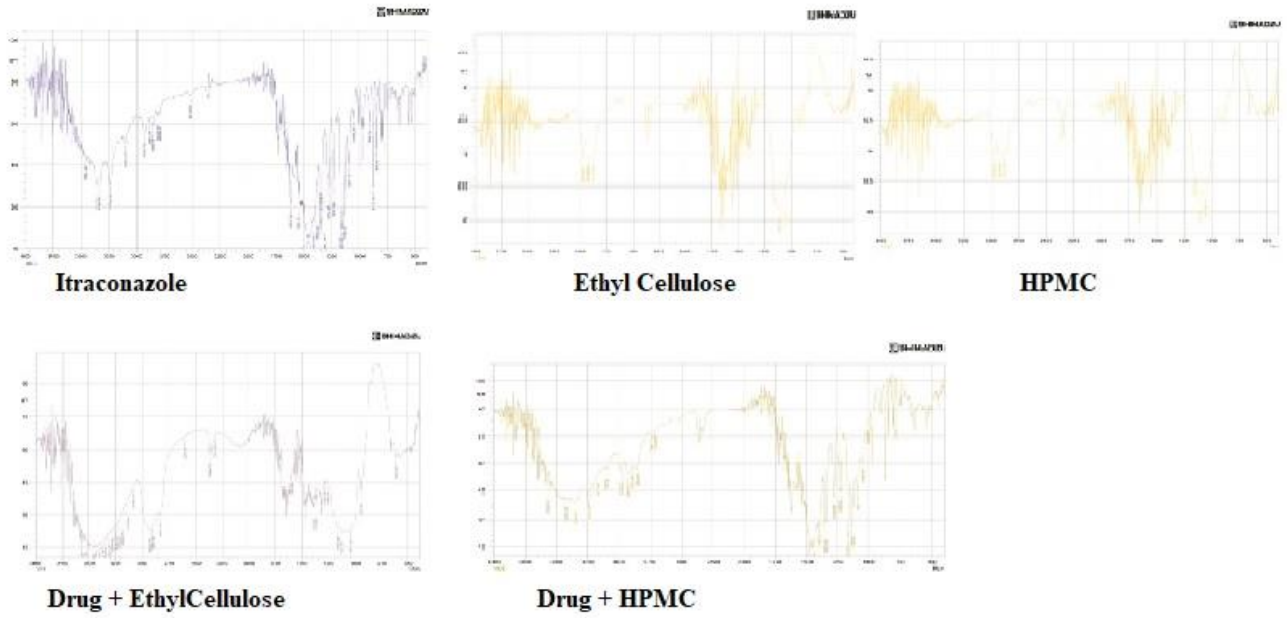


Figure 1. FTIR Spectrum of Drug and Excipients

Table 2. Interpretations of FTIR

Observed peak	Characteristic peak	Bond	Functional Groups
ITRACONAZOLE			
3462.22	3300-3500	-N-H-	Amines
3342.64	3300-3500	-N-H-	Amines
2933.73	2700-3300	C-H Stretch	Aromatics
2883.58	2700-3300	C-H Stretch	Aromatics
1521.84	1500-1600	-C-C	Aromatic rings
348.24	285-400	-N=N-	Azo group
ETHYL CELLULOSE			
2974.23	2500-3000	C-H Stretch	Aromatics
1159.22	900-1300 800-1200	C-O Stretch C-C Stretch	Alcohols Aromatics
1056.99	900-1300 800-1200	C-O Stretch C-C Stretch	Alcohols Aromatics
HPMC			
336.85	3200-3400 3000-3700	O-H Stretch N-H Stretch	Carboxylic acids 1^{o} &2^{o} amines
3088.03	3010-3100	=C-H -	Alkenes
2922.16	2700-3300 2850-2960	C-H Stretch -C-H -	Aromatics Alkanes
DRUG + ETHYL CELLULOSE			
3346.50	3000-3700 3000-3700	O-H Stretch N-H Stretch	Hydrogen bonded alcohols and phenols
2974.23	2700-3300	C-H Stretch	Aromatics
1400.32	600-1500	-C-H-	Alkanes
DRUG + ETHYL CELLULOSE + HPMC			
562.52	500-600	C-Br Stretch	Alkyl halides
3520.09	3300-3600 3000-3700	C=O Stretch O-H Stretch	Hydrogen bonded alcohols and phenols
2972.31	2700-3300	C-H Stretch	Aromatics
2873.94	2700-3300	C-H Stretch	Aromatics

Differential scanning calorimetry

The pure drug like DSC specimen like spectra a Exothermic peak has been 122.5^{0}c but also -10.65 mw. A mix specimen consists of opioid (Itraconazole), Ethyl cellulose, HPMC the exothermic peak is 121.9^{o}C & -9.29 mw, the endothermic peak of the mixture 286.2 ^{o}C

& -7.50 mw, the compatibility like opioid as well as excipients shows there is no congeniality within formulation as shown in Table 3**.** It is relevant for performing formulation of Nanocapsules. The DSC spectra as shown in figure 2.

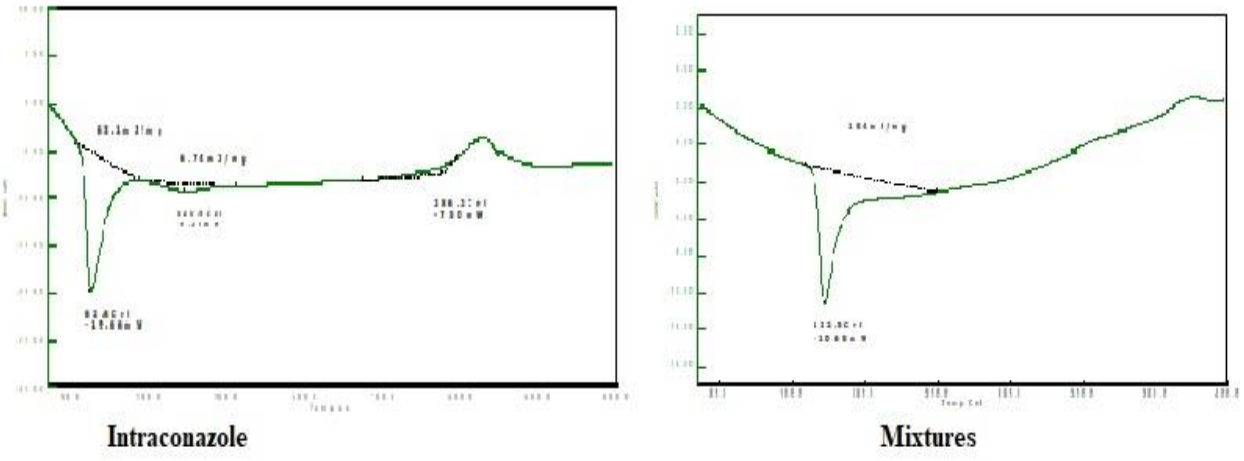


Figure 2. DSC spectrum of pure drug Itraconazole

Table 3. Interpretation of DSC Spectrum

Drug & Excipients	Exothermic peak	Endothermic peak
Itraconazole	122.5^{o}c & -10.65 mw	----------
Drug+ethyl cellulose+Hpmc	121.9^{o}c & -9.29 mw	286.2^{o}C & -7.50 mW

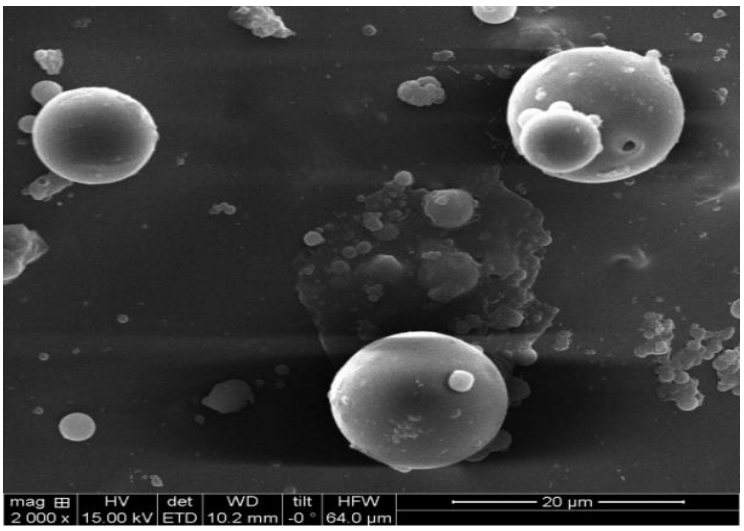
Morphology of the particles:

The following method have been utilized for determining size of particles, size distribution and morphology for Itraconazole Nanocapsules.

SEM

Morphology and structure of Nanocapsules have been described by utilising scanning electron microscopy (SEM) but also photomicrographs have been considered there as appropriate magnifications. The images of an optimized composition have been considered through Scanning electron microscopy can be seen in the Figure 3.

Shape and surface morphology:



Figures 3. SEM Samples of Best formulations of F 8

Evaluation of Itraconazole Nanocapsules

Percentage Yield

The production yield of Nanocapsules of Itraconazole utilisng HPMC & Ethyl cellulose results as shown in Table 4.

Drug entrapment efficiency (%EE)

Percentage entrapment efficiency of F 1- 54.3%, F2- 87.2%, F3- 68%, F 4 – 59%, F 5- 63.7%, F 6- 60.9%, F 7- 58.9, F 8-91.3, The F 8 shows the good formulation & high efficiency. Results have been shown within Table 4.

Entrapment Loading (%EL)

Percentage entrapment loading of F 1- 56.9 %, F2- 87,8%, F3- 84.2%, F 4 – 71.8%, F 5- 70.5%, F 6- 68.9%, F 7- 64.9, F 8- 97.8. The F 8 shows the good formulation & high efficiency. Results have been shown within Table 4.

Particle size

Particle size distribution of Nanocapsules represents through F 1 (80µm), F 2 (62 µm), F3 (98 µm), F4 (51 µm), F 5 (90 µm), F 6 (90 µm), F 7 (70 µm), F 8 (22 µm). Formula have been shown within given Table 4.

Equilibrium swelling studies of Nanocapsules

A preweighed amount (100 mg) of Nano capsules has been positioned through Phosphate buffer (pH7.4) as well as permitted of about swell to either a steady weight. A Nanocapsules have been eliminated as well as blotted as for filter paper, but also about there alters through weight have been calculated outcomes can be seen in table 4.

Percentage drug content Determination:

Drug content dispersion like Nanocapsules represents this implied a certain drug content is F 1 (65.9%), F 2 (69.3 %), F3 (90.4%), F4 (89.8%), F 5 (75.3 %), F 6 (85.3 %), F 7 (88.6 %), F 8 (98.4%) as shown in given Table 4 .

Table 4. Evaluation Parameters of Itraconazole Nanocapsules

Formulation code	Percentage yield (%)	Entrapment efficiency	Entrapment Loading Efficiency	Particle size (µm)	Swelling Index (Sec)	Percentage drug content determination (%)
F1	83.44	54.3	56.9	80	0.6Sec	65.9
F2	81	87.2	87.8	62	0.3 Sec	69.3
F3	73.22	68	84.2	98	0.2Sec	90.4
F4	78.87	59	71.8	51	0.8 Sec	89.8
F5	88.91	63.7	70.5	90	0.4 Sec	75.3
F6	81.43	60.9	68.9	90	0.2 Sec	85.3
F7	79	58.9	64.9	70	0.4Sec	88.6
F8	86.54	91.3	97.8	22	1.6 Sec	98.4

In-vitro dissolution Studies:

For understanding the mechanism of drug release rate kinetics of the drug from dosage forms, the *in vitro* drug dissolution obtained data has been equipped to numerous mathematical equations such like zero order, 1st order, Higuchi matrix, as well as Korsmeyer Peppas model. The values are complied in Table 6-7. The % drug release with data to various kinetic models for different Nanocapsules formulations has been presented within figure 5-8.

Table 5. *In-Vitro* dissolution Studies

Sl.no	Time	% of Drug release							
		F1	F2	F3	F4	F5	F6	F7	F8
1	5	1.61	3.07	6.81	7.72	11.62	13.21	14.58	15.38
2	10	4.58	6.89	9.32	12.41	15.53	16.89	19.28	27.07
3	15	6.71	8.51	11.61	14.58	19.27	23.17	23.17	34.78
4	20	7.59	11.62	14.58	19.29	23.22	23.98	27.81	38.71
5	25	11.61	15.51	19.28	23.21	27.07	36.4	37.78	46.41
6	30	15.38	27.08	30.8	35.41	37.09	38.55	42.51	50.33
7	35	27.07	34.9	34.9	38.59	39.38	40.99	45.72	54.22
8	40	30.8	42.39	51.1	54.6	62.72	71.2	68.58	61.78
9	45	38.58	50.33	54.8	61.91	70.31	76.61	77.31	88.87

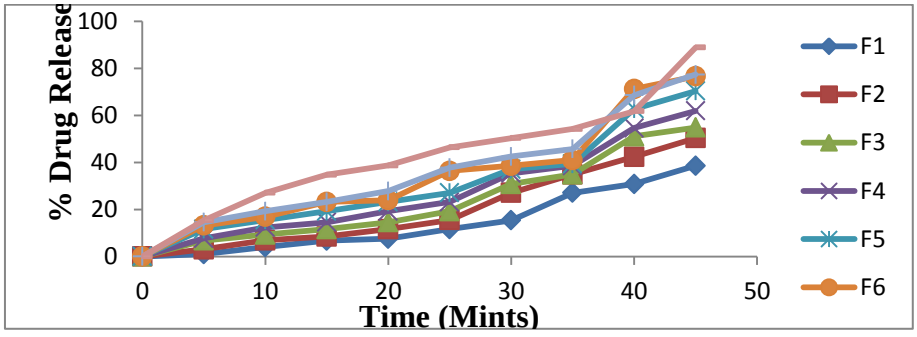


Figure 4. *In vitro* dissolution studies of Itraconazole Nanocapsules

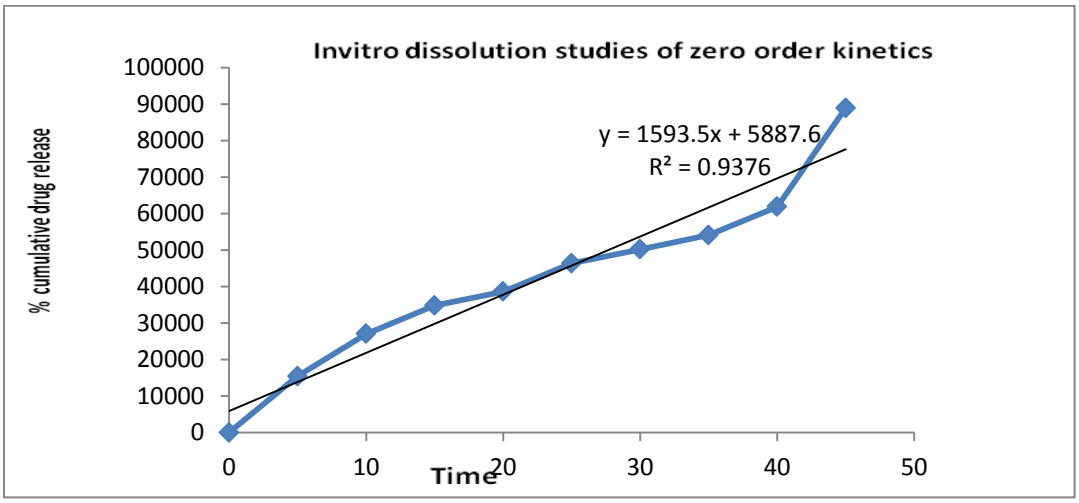


Figure 5. F 8 of *In vitro* dissolution studies of zero order kinetics

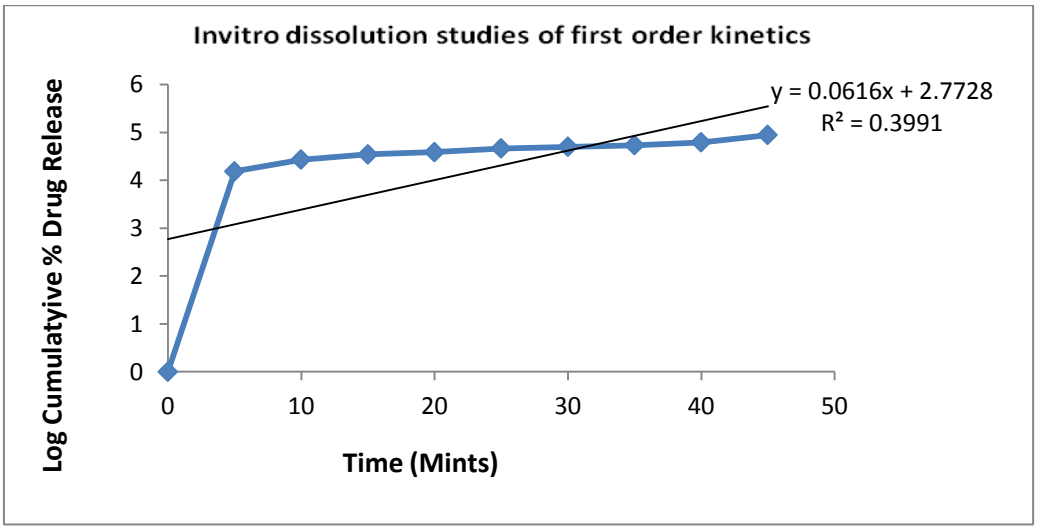


Figure 6. F 8 of *In vitro* dissolution studies of First order kinetics

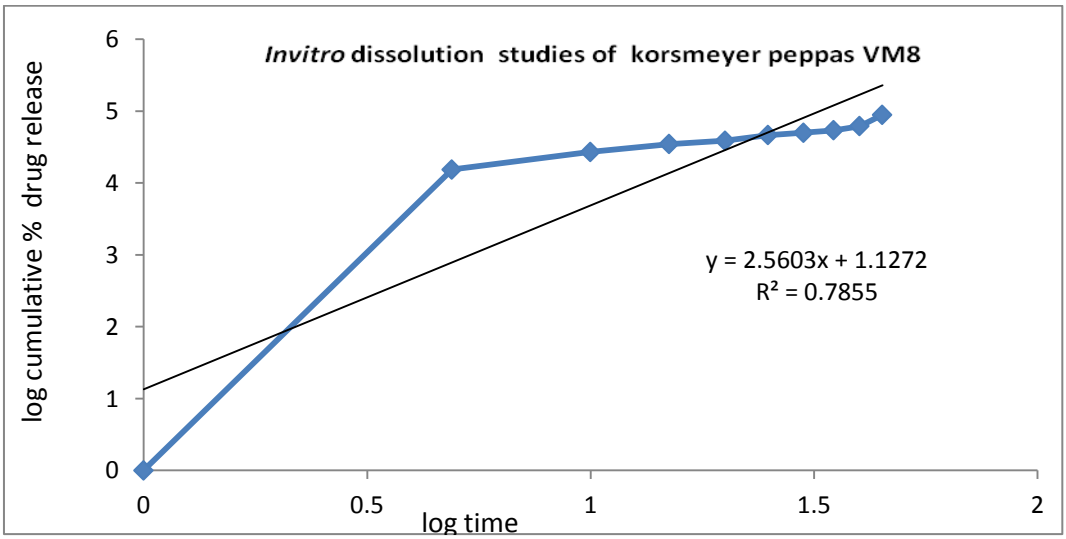


Figure 7. F 8 of *In vitro* dissolution studies of korsmeyer peppas

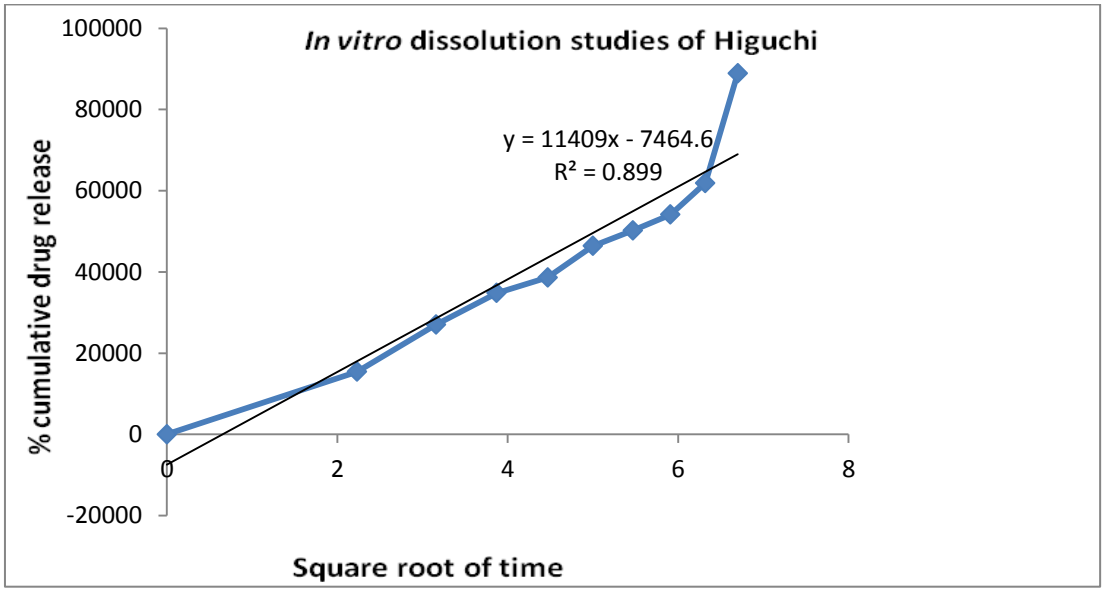


Figure 8. F8 of *In vitro* dissolution studies of Higuchi

Table 6. Release kinetics of Itraconazole Nanocapsules (F1 to F5)

Model	Equation	F 1		F 2		F 3		F 4		F 5	
		R^2	m	R^2	m	R^2	M	R^2	m	R^2	M
Zero order	Mo-Mt=kt	0.655	69.4	0.939	1123	0.007	15.93	0.202	72.88	0.928	1414
First order	InM=InMo	0.494	0.061	0.540	0.067	0.257	0.038	0.352	0.044	0.438	0.062
Higuchi's Matrix	$M_0 - M_t = kt1/2$	0.516	4508	0.767	7420	0.023	212.0	0.189	515.5	0.803	9618
Korsmeyer-Peppar	log (M_0-M_t)= log k + n log$t$	0.835	2.354	0.884	2.545	0.572	1.709	0.663	1.813	0.806	2.517

Table 7. Release kinetics of Itraconazole Nanocapsules (F6 to F9)

Model	Equation	F 6		F 7		F 8	
		R^2	m	R^2	m	R^2	M
Zero order	Mo-Mt=kt	0.917	15.49	0.949	154.4	0.937	1593
First order	InM=InMo	0.481	0.052	0.465	0.051	0.399	0.061
Higuchi's Matrix	$M_0 - M_t = kt1/2$	0.798	1057	0.848	1067	0.899	11409
Korsmeyer-Peppar	log (M_0-M_t)= log k + n log$t$	0.835	2.032	0.827	2.033	0.785	2.560

4. Conclusion

The aim of present study has been to establish Nanocapsules like Itraconazole such as sustained drug-delivery. Out from findings this seem a certain composition f8 has been did find being the outstanding morphometric qualities, % yield of microsphere like finest composition has been did find to also be f8 (86.54%). Encapsulation efficiency like finest composition has been did find of being (91.3%), drug loading efficiency like finest composition has been did find of being (97.8%), swelling index finest composition has been did find of being (1.6sec), size of the particles of finest composition has been did find to be (22µm), drug content determination like finest composition has been did find of being (98.4) and in vitro drug release has been equipped as for variety discharge kinetic research of a consistent manner to consistent fashion around longer length of time for 45 mnts. This was discovered a certain concentration like ethyl cellulose impacted all of the evaluation parametric substantially. Thus the fully ready Nanocpasules like Itraconazole could demonstrate to also be possible candidate such as effective and safe sustained drug delivery.

Acknowledgements

I would like to express my gratitude to Himalayan Journal of Health Sciences who gave me the opportunity to publish the article.

Financial Disclosure statement: The author received no specific funding for this work.

Conflict of Interest

The author declares that there is no conflict of interest regarding the publication of this article.

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