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SUGAR-FREE RECONSTITUTED DRY SYRUP OF AZITHROMYCIN DIHYDRATE USING FENUGREEK MUCILAGE AS NATURAL SUSPENDING AGENT

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Abstract : Reconstitutable oral dry syrups are vital pharmaceutical dosage forms designed for medications that exhibit instability in aqueous environments, most notably antibiotics such as amoxicillin, cephalexin and ciprofloxacin. These formulations consist of dry mixtures of finely divided insoluble particles, typically ranging from 0.5 to 5 in diameter, intended to be suspended in a vehicle at the time of dispensing. This review evaluates the development of sugar-free systems to accommodate paediatric, geriatric and diabetic populations while utilizing natural suspending agents like fenugreek seed mucilage (Trigonella foenum-graecum), acacia and xanthan gum. Natural agents are prioritized due to their biodegradability, non-toxicity and superior thixotropic properties compared to synthetic alternatives. The article details comprehensive preformulation, formulation and post-formulation methods. Key evaluation parameters, containing micromeritic flow properties (Angle of Repose, bulk/tapped density), sedimentation volume (F) and in-vitro dissolution kinetics, are discussed. Findings indicate that natural polymers grant excellent physical stability and dose regularity, ensuring a long shelf life of at least two years in dry form

Key Words: Dry syrup, Natural suspending agent, Sugar-free formulation.

1.INTRODUCTION

Oral route of administration is the most widely favored direction due to patient convenience, safety and ease of administration. However, conventional solid dosage forms such as tablets and capsules are often unsuitable for pediatric and geriatric patients due to difficulty in swallowing [1].Liquid dosage forms overcome swallowing complications but frequently suffer from poor stability, microbial growth and shorter shelf life [2].To overcome these problems, dry syrups were developed in which the drug is supplied in dry form and reconstituted with water immediately before use [3]. Reconstitution dry syrups offer improved chemical stability, reduced microbial contamination, ease of transport and extended shelf life compared to liquid syrups . Azithromycin dihydrate is a semi-synthetic azalide antibiotic derived from erythromycin and belongs to the macrolide class [4].

Suspending agents play a vital role in reconstituted suspensions by maintaining uniform dispersion of drug particles throughout the dosing period [5]. Synthetic suspending agents such as sodium CMC and xanthan gum are commonly used but may cause gastrointestinal irritation and are less eco-friendly [6]. Therefore, natural suspending agents obtained from plant sources are increasingly explored due to their safety and biodegradability. Fenugreek (Trigonella foenum-graecum) seeds contain a high amount of mucilage composed mainly of galactomannan polysaccharides[7]. Fenugreek mucilage exhibits excellent swelling, viscosity-enhancing and suspending properties, making it suitable for pharmaceutical use . It is biodegradable, biocompatible, non-toxic and economical, which makes it a promising substitute to synthetic polymers [8].

2.MATERIALS AND METHODS

2.1.LIST OF CHEMICALS AND EQUIPMENTS

The materials used for the formulation involved Azithromycin dihydrate obtained from India Mart and Fenugreek seed mucilage obtained from a local source. D-Mannitol and Potassium sorbate were purchased from Isochem. Stevia was obtained from Organic India Pvt. Ltd. Citric acid and Sodium citrate were supplied by S.D. Fine Chem Ltd. Disodium EDTA and Polysorbate 80 were procured from Merck Ltd. Colloidal silicon dioxide and Magnesium stearate were obtained from Loba Chemie Pvt. Ltd. Distilled water used in the formulation was sourced from the laboratory supply.

The equipment used in the study included an electronic balance (PG-620) manufactured by Shimadzu Corporation for accurate weighing. A porcelain mortar and pestle supplied by Borosil was used for trituration. Sieving was carried out using Sieve No. 60 (ASTM standard) from Jayant Test Sieves. Drying operations were performed using a standard hot air oven from Lab India. The pH of the formulations was measured using a digital pH meter from Eutech Instruments. Viscosity measurements were carried out using a Brookfield LV viscometer from Brookfield Engineering. A graduated glass measuring cylinder from Borosil was used for volume measurements and a UV-Visible spectrophotometer (UV-1800) from Shimadzu was employed for analytical studies.

2.2.METHODOLOGY

A. Preparation of Fenugreek Seed Mucilage (Natural Suspending Agent)

Fenugreek (Trigonella foenum-graecum) seeds were procured from a local market and cleaned thoroughly to remove dust and foreign matter.The cleaned seeds were soaked in distilled water (1:20 w/v) for 12–24 hours at room temperature to allow swelling and mucilage release.The swollen seeds were triturated using a mortar and pestle and the slurry was filtered through a muslin cloth to separate the mucilaginous extract.The filtrate was treated with three times its volume of acetone with continuous stirring to precipitate the mucilage.The precipitated mucilage was collected, dried at 40–45 °C, powdered, passed through sieve no. 80 and stored in a desiccator for further use[9].

Figure no.1: steps involved in drying and pulverization of extracted mucilage

B. PREPARATION OF SUGAR-FREE DRY SYRUP BLEND

All ingredients were accurately weighed as per the formulation composition Azithromycin dihydrate was triturated gently with mannitol to ensure uniform distribution and reduction of agglomerates . The dried fenugreek seed mucilage was added gradually to the drug–diluent mixture and blended uniformly to impart suspending properties after reconstitution . Addition of Sweetener and Buffer Stevia was added as a sugar-free sweetening agent. Sodium citrate and citric acid were incorporated to maintain pH stability and improve palatability Disodium EDTA, potassium sorbate, polysorbate-80 and colloidal silicon dioxide were added sequentially and mixed thoroughly to enhance stability, wetting and flow properties Finally, magnesium stearate was added and gently blended to improve powder flow without over-mixing . The final blend was passed through sieve no. 60 to obtain a uniform, free-flowing dry powder suitable for reconstitution[10] .

FORMULATION TABLE

Sugar-Free Reconstitutable Dry Syrup of Azithromycin Dihydrate Final Volume after Reconstitution: 60 mL

Label Claim

Azithromycin 200 mg / 5 mL

Total drug required for 60 mL: $\frac{200mg}{5ml}$ X 60ml = 2400 mg

Table no.1: Formulation table

INGREDIENTS	RDDA1 (mg)	RDDA2 (mg)	RDDA3 (mg)
Azithromycin dihydrate	2000 mg	2000 mg	2000 mg
Fenugreek seed mucilage	600 mg	650 mg	700 mg
D-Mannitol	15000 mg	15000 mg	15000 mg
Stevia	120 mg	120 mg	120 mg

Citric acid	90 mg	90 mg	90 mg
Sodium citrate	180 mg	180 mg	180 mg
Disodium EDTA	30 mg	30 mg	30 mg
Colloidal Silicon Dioxide	60 mg	60 mg	60 mg
Potassium Sorbate	90 mg	90 mg	90 mg
Polysorbate 80	60 mg	60 mg	60 mg
Talcum powder	30 mg	30 mg	30 mg
Vanillin	500 mg	500 mg	500 mg

2.3.PREFORMULATION

Organoleptic properties

The organoleptic evaluation of the drug substance revealed that it appeared as a white to off-white crystalline powder. The colour was observed to be white or slightly off-white in nature. The sample was found to be odourless or exhibited a faint characteristic odour. On taste evaluation, it showed a strongly bitter taste, which is typical for many macrolide antibiotics. The texture was identified as fine and crystalline, indicating uniform particle characteristics suitable for formulation development [10].

Solubility study

Solubility study was performed for each one of the excipients by using water and ethanol (95%) and buffer .50g of each materials was weight and dissolved into 100 ml of each one of the solvent for a specific amount of time. The result were absorbed and recorded as per reference[10].

Melting point

The melting point of the drug was performed by capillary method. In this, drug was filled in the capillary tube sealed at one end to a height of 3 mm from closed end and capillary was introduced into digital melting point apparatus . The temperature range at which drug melt was noted down[10] .

FTIR Spectroscopy

Fourier Transform Infrared (FTIR) Spectroscopy: FTIR is a powerful tool for chemical recognition and examining the interface between a drug and its carriers to ensure no deleterious interactions occur. Samples are typically prepared using the potassium bromide (KBr) pellet method, where approximately 5 mg of the sample is mixed with 50–100 mg of IR-grade KBr powder and compacted under vacuum/high pressure to form a transparent disc. The resultant disc is scanned in the infrared range of 500 to 4000 cm^{-1}. Compatibility is confirmed by comparing the spectra of the pure drug with its physical mixtures; the preservation of characteristic peaks (such as O-H or C=O stretching) and the absence of new peaks indicate that the drug and excipients are compatible

UV-spectroscopy

Finding the A Max the wavelength at which a medicine absorbs the most light is known as its A max. The A max of a substance is a unique property that is hard to change. A stock solution of 1 mg/ml was prepared by dissolving 100 mg of azithromycin in a tiny amount of methanol and then diluting it further with 100 ml of phosphate buffer (pH 6.8). This was done in order to determine the drug's A max. The stock solution was significantly diluted to produce solutions in the 2-12 µg/ml range. Scanning in the 200-400 nm region allowed us to determine the solution's 2 max[10].

Zeta potential

Zeta potential measurement: The zeta potential is measured in triplicates in multimodal mode. Prior to the measurement, Suspension is diluted with distilled water and the measurements are taken in triplicate[10].

2.4.EVALUATION OF BEFORE RECONSTITUABLE ORAL SUSPENSION

BULK DENSITY

The predetermined or pre weighed mass of the powder blend volume was measured for determination of bulk density .

Bulk Density (Db) = (M) / (Vo)

Where,

M =Weight of the powder blend
Vo = Apparnt volume of the powder blend[11]

TAPPED DENSITY

The measuring cylinder which contains a powder sample was mechanically tapped. The initial volume was observed before tapping, the cylinder was mechanically tapped and volume readings were taken until little further volume change was observed.

Tapped density (Dt) = (M) / (Vf)

Where,

M = weight of the powder blend.
Vf = Final volume of the powder blend[11].

CARR'S INDEX OR COMPRESSIBILITY INDEX

The Carr's Index or Compressibilty Index was calculated by the formula

I = Dt -Db / Dt ×100

Where,

Db=Bulk density

Dt = Tapped density[11].

ANGLE OF REPOSE (θ)

The angle of repose of powder blend was determined by using employing fixed funnel method

Tan θ= h/r,

Where,

h = height of the heap.

r = radius of the heap[11].

2.5.EVALUATION OF AFTRE RECONSTITUABLE ORAL SUSPENSION

Rheological behaviour

The Brookfield viscometer is used to determine the rheological properties of the reconstituted solution[12].

Deposit behaviour

a)Redispersibility

Within a week of seven days of storage, the Redispersibility of a preparation is determined by measuring the number of strokes necessary to redisperse the created sediment. (not more than 100 strokes = Redispersibility)[12].

b) Sedimentation Volume Ratio (SVR)

The sedimentation volume of suspension is simply the ratio of the balance capacity of the sediment, Vu, to the overall volume, Vo, of the suspension, i.e., F= Vu/Vo. For any pharmacological solution, F is usually between 0 and 1. The F value gives qualitative information regarding the suspension's physical stability[12].

Drug content

With 100ml liquid, the required amount of medicine combination is separated and filtered through a nylon filter membrane. UV Spectroscopy is used to measure the absorbance of the solution, which is diluted to filtered water using solvent. The drug concentration is calculated using the solvent calibration graph[12].

pH values

A pH meter was used to determine the pH of the suspension[12].

Taste evaluation of optimized formulation

The taste evaluation was performed using taste panel of 3 volunteers in the age group Of 19-25yrs. 5ml of each formulation was held in the mouth for 20 seconds by each volunteer and the bitterness level was recorded[12].

Dissolution studies

The dissolution studies were performed using a US Pharmacopeia XXIV type II dissolution test apparatus. The samples equivalent to 100 mg Azithromycin Dihydrate were placed in a dissolution vessel containing 900 mL of phosphate buffer (pH 6.0) maintained at 37.0 ± 0.5oC and stirred at 100 rpm. Samples were collected periodically and replaced with a fresh dissolution medium. After filtration, concentration of Azithromycin Dihydrate was determined spectrophotometrically at 215 nm [13].

In-vitro drug release kinetics

The in-vitro dissolution data were fitted to zero-order, first-order, Higuchi and Korsmeyer–Peppas kinetic models and the regression coefficient (R^2) and release exponent (n) values were used to determine the drug release pattern and mechanism. Fickian diffusion occurs when drug release is controlled purely by diffusion through the polymer matrix ($n \leq 0.45$), whereas non-Fickian (anomalous) diffusion occurs when drug release is governed by a combination of diffusion and polymer swelling or erosion ($0.45 < n < 0.89$ [13]

3.RESULT AND DISCUSSION

3.1.PREFORMULATION STUDIES

ORGANOLEPTIC EVALUATION

Table no.2: Organoleptic characteristics

S.NO.	CHARACTERISTIC	RDDA1	RDDA2	RDDA3
1	Appearance	White crystalline powder	White to off-white powder	Slightly off-white crystalline
2	Colour	White	White	Off-white
3	Odour	Odourless	Slightly characteristic	Odourless
4	Taste	Bitter	Slightly bitter	Masked (less bitter)
5	Texture	Fine, crystalline	Fine powder	Fine, free flowing

All three formulations showed acceptable organoleptic properties. RDDA3 showed improved taste masking compared to RDDA1 and RDDA2, indicating better suitability for dry syrup formulation.

SOLUBILITY STUDIES

Table no.3: solubility profile

S.NO.	CHARACTERISTIC	RDDA1	RDDA2	RDDA3
1	Solubility in Water	Sparingly soluble	Slightly soluble	Slightly soluble
2	Solubility in Ethanol	Soluble	Soluble	Soluble
3	Solubility in Phosphate buffer pH 6.8	Slightly soluble	Moderately soluble	Moderately soluble
4	Solubility in Methanol	Soluble	Soluble	Soluble

All formulations showed poor aqueous solubility, confirming the suitability of azithromycin dihydrate for dry suspension formulation. RDDA2 and RDDA3showed slightly improved solubility in buffer compared to RDDA1.

MELTING POINT DETERMINATION

Using the capillary method , the melting point of azithromycin dihydrate was ascertained. it was discovered that azithromycin dihydrate had a melting point of 116^0C it meets requirements, demonstrating the drug samples purity .The observed melting point closely matched the reported value, indicating the purity and identity of the drug.

FTIR

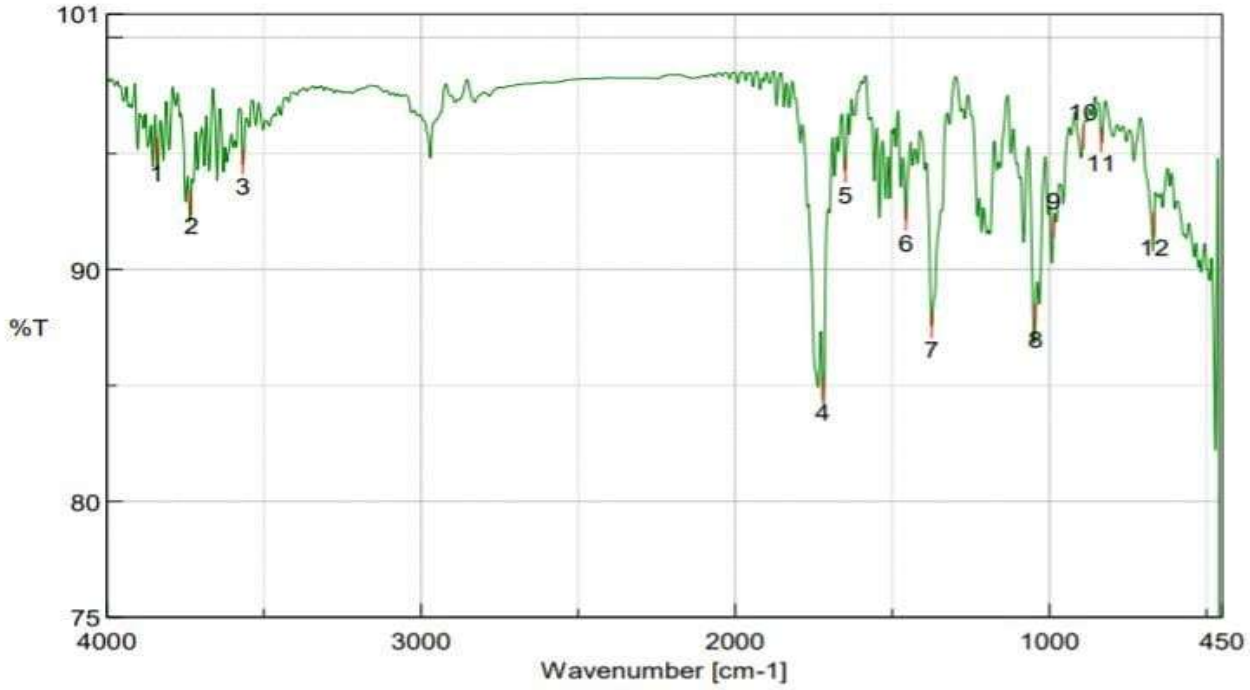

Figure no:02 FTIR of Azithromycin

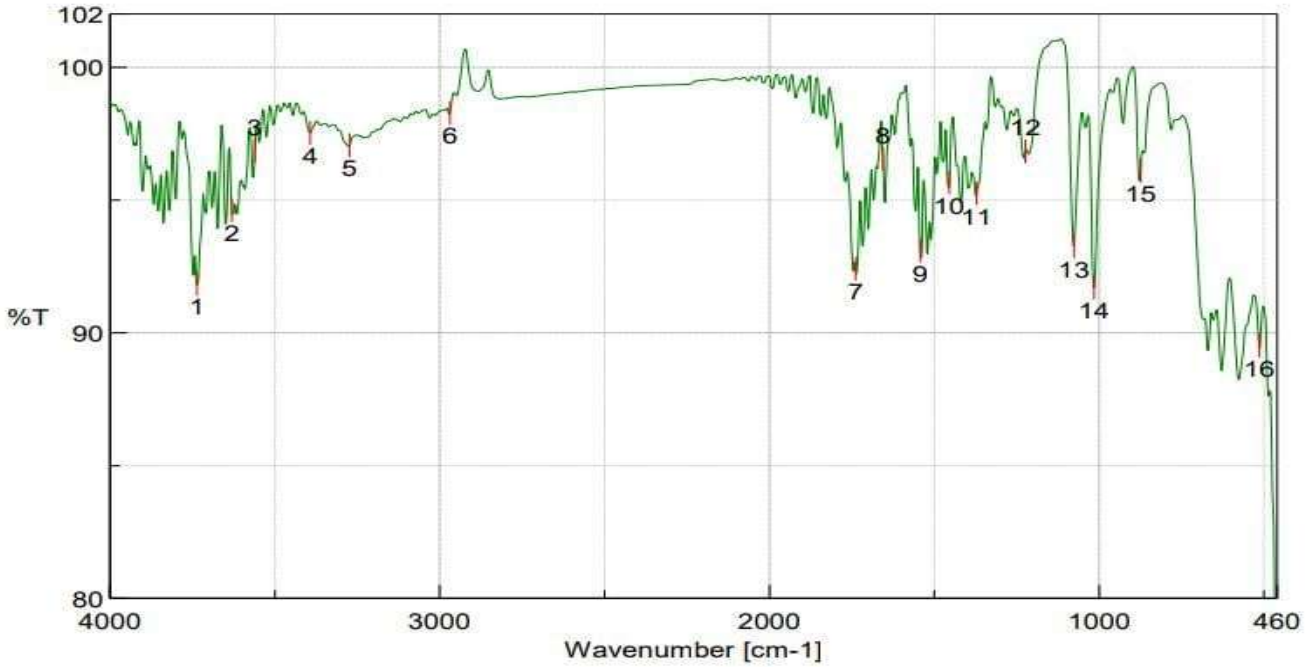

Figure no:03 FTIR of white powder with azithromycin

Table.no 4: FTIR of white powder with azithromycin

Peak No.	**Position (cm^{-1})**	**Intensity (%T)**
1	3736.4	91.8362
2	3630.34	94.6084
3	3560.91	96.8387
4	3393.14	97.5217
5	3273.57	97.0642

6	2968.87	98.2779
7	1738.51	92.4105
8	1655.59	96.5285
9	1542.77	93.0958
10	1454.06	95.6526
11	1371.14	95.2534
12	1224.58	96.8214
13	1077.05	93.2599
14	1015.34	91.7009
15	874.56	96.105
16	514.901	89.5114

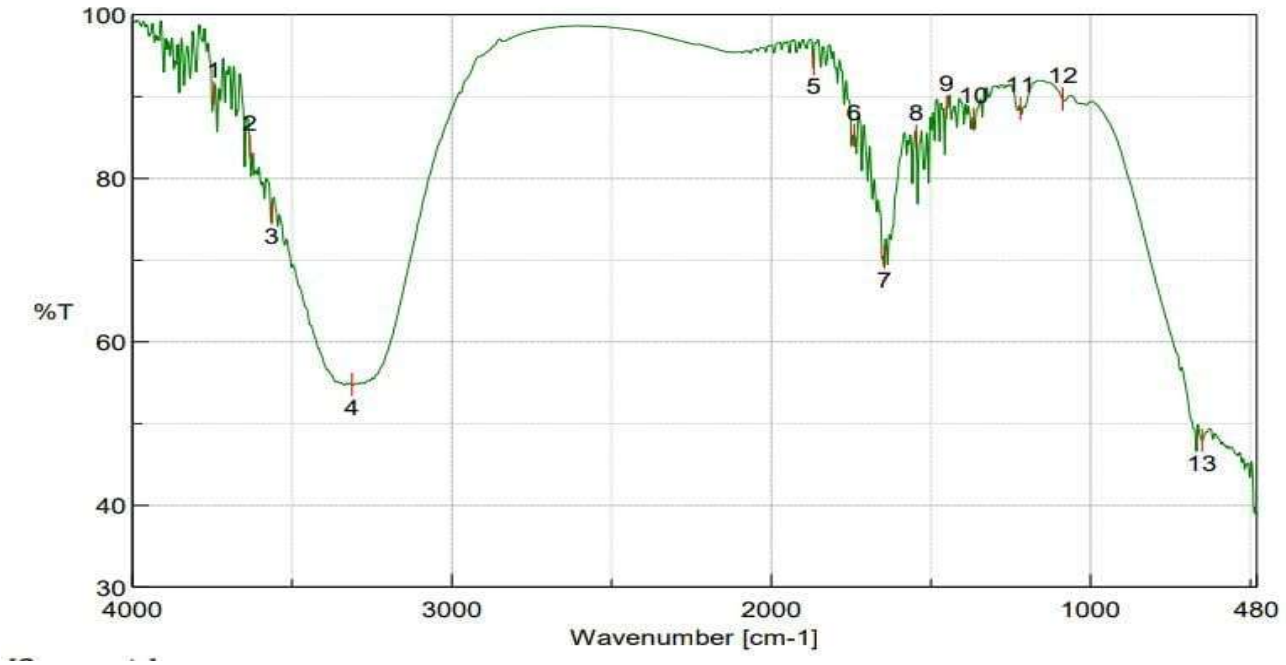

Figure no:04 FTIR of liquid with azithromycin

Table.no 5: FTIR of liquid with azithromycin

Peak No.	**Position (cm^{-1})**	**Intensity (%T)**
1	3744.12	90.4074
2	3632.27	83.8534
3	3563.81	75.7288
4	3312.14	54.8018
5	1866.76	94.02
6	1740.44	85.2222
7	1644.98	70.3591
8	1546.63	85.1348

9	1451.17	88.6785
10	1366.32	87.2012
11	1219.76	88.4849
12	1086.69	89.6803
13	650.858	47.946

The FTIR spectra of the formulations (Memory-4, Memory-5 and Memory-7) showed all the characteristic absorption bands of azithromycin dihydrate without the appearance of new peaks or significant shifts.

A broad absorption band observed in the region of 3400–3500 cm^{-1} corresponds to O–H stretching vibrations, indicating the presence of hydroxyl groups and the dihydrate nature of azithromycin, as well as hydroxyl groups of fenugreek mucilage. The peaks appearing around 2920–2850 cm^{-1} are attributed to aliphatic C–H stretching, confirming the macrolide backbone of the drug. The characteristic sharp peak in the region of 1700–1730 cm^{-1} represents C=O stretching of the lactone ring, which is a key structural feature of azithromycin and was retained in all formulations.

Absorption bands observed around 1380–1400 cm^{-1} correspond to C–N stretching vibrations of the tertiary amine group present in azithromycin. Peaks in the region of 1050–1150 cm^{-1} indicate C–O and C–O–C stretching vibrations, confirming the presence of ether and glycosidic linkages. Minor variations in peak intensity were observed, which can be attributed to physical mixing and hydrogen bonding between the drug and fenugreek mucilage, rather than chemical interaction.

FTIR studies demonstrate that the drug remains chemically stable and compatible, supporting the suitability of fenugreek mucilage as a natural suspending agent in the developed dry syrup formulation.

UV SPECTROSCOPY

UV spectroscopic analysis (200–270 nm) showed a gradual increase in absorbance from 0.22 at 200 nm to a maximum of 0.92 at 215 nm, confirming the λmax at 215 nm due to electronic transitions of chromophoric groups. Beyond 215 nm, absorbance steadily decreased to 0.10 at 270 nm without additional peaks, indicating good spectral purity and absence of interference. The well-defined λmax at 215 nm confirms the drug's identity and suitability for quantitative estimation.

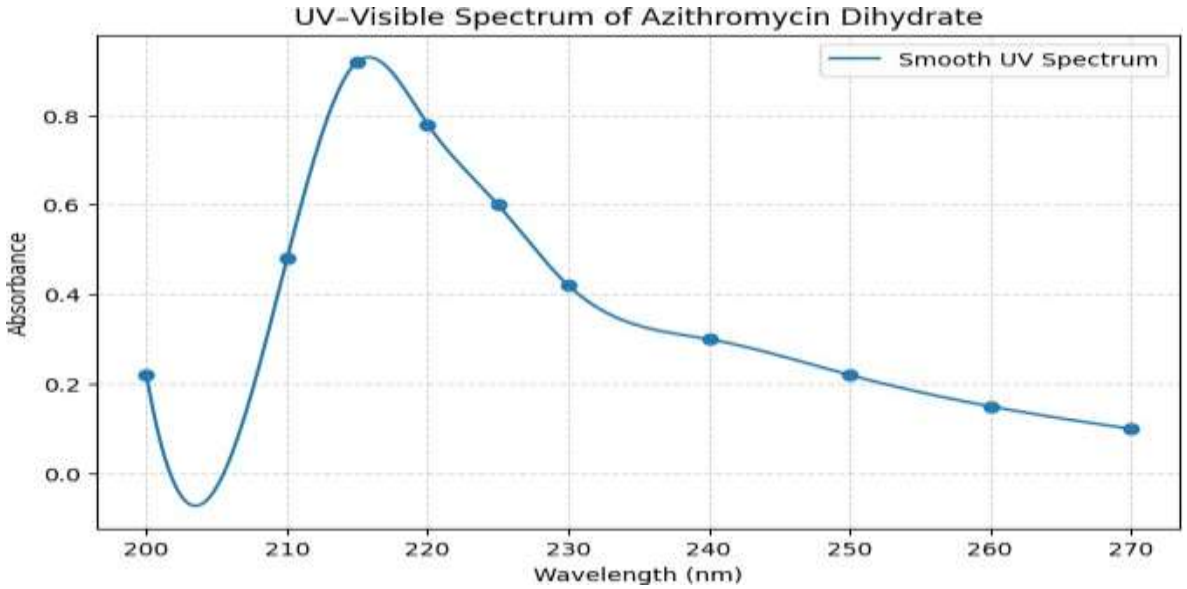

Figure No.5:UV spectrum of azithromycin dihydrate

Table no.6: UV spectral of azithromycin dihydrate

S.NO	WAVELENGTH (nm)	ABSORBANCE
1	200 nm	0.2210
2	210 nm	0.4866
3	215 nm	0.9201
4	220 nm	0.7854

5	225 nm	0.6033
6	230 nm	0.4211
7	240 nm	0.3075
8	250 nm	0.2210
9	260 nm	0.1543
10	270 nm	0.1001

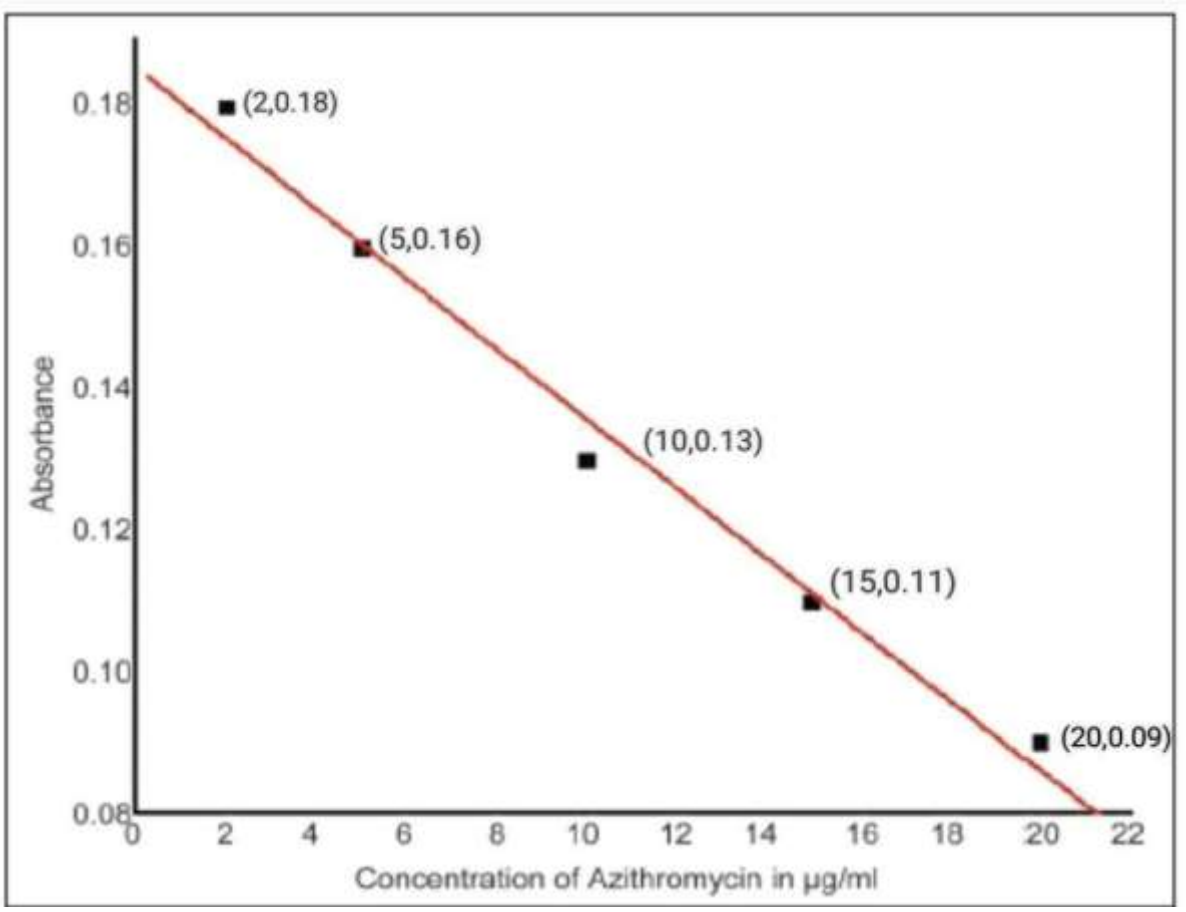

Figure no.6:Calibration curve of azithromycin dihydrate

Table no.7: Concentration vs Absorbance Data for Azithromycin Dihydrate

S.NO	CONCENTRATION OF AZITHROMYCIN (µg/mL)	ABSORBANCE
1	2 µg/mL	0.1866
2	5 µg/mL	0.1642
3	10 µg/mL	0.1301
4	15 µg/mL	0.1133
5	20 µg/mL	0.0902

3.2.EVALUATION

BEFORE RECONSTITUTION

Table no.8:evaluation parameters of formulations

PARAMETERS	RDDA1	RDDA2	RDDA3
Bulk density(g/ml)	±0.48 g/ml	±0.50 g/ml	±0.52 g/ml
Tapped density(g/ml)	±0.60 g/ml	±0.61 g/ml	±0.62 g/ml
Carr's index(%)	20.0 %	18.0 %	16.1 %
Angle of Repose	28.5°	26.2 °	24.8 °
Viscosity(cP)	±620 cP	±740 cP	±880 cP
Sedimentation Volume Ratio	±0.68	±0.74	±0.82
Redispersibility	85	70	55
pH	6.2	6.4	6.6
Drug content(%)	96.4 %	98.1 %	99.2 %

The evaluation results showed a gradual improvement in the properties of formulations RDDA1, RDDA2 and RDDA3. Bulk and tapped density values increased slightly, indicating better packing characteristics. Carr's index decreased from 20.0% to 16.1% and angle of repose decreased from 28.5° to 24.8°, suggesting improved flow properties with RDDA3 showing the best flow. Viscosity increased from 620 cP to 880 cP, which contributed to enhanced suspension stability, as reflected by the increase in sedimentation volume ratio from 0.68 to 0.82. Redispersibility time decreased from 85 to 55 seconds, indicating easier redispersion of the suspension. The pH values remained within an acceptable range of 6.2–6.6, suitable for oral administration. Drug content increased from 96.4% to 99.2%, confirming uniform drug distribution, with RDDA3 identified as the optimized formulation.

AFTER RECONSTITUTION

Table no.9:evaluation parameters of formulations

Parameter	RDDA1	RDDA2	RDDA3
Reconstitution Time (sec)	85 sec	65 sec	45 sec
Sedimentation Volume Ratio	±0.68	±0.74	±0.82
Redispersibility (No. of Strokes)	85	70	55
pH	6.2	6.4	6.6
Viscosity (cP)	±620 cP	±740 cP	±880 cP
Drug Content (%)	96.4%	98.1%	99.2%
Taste Evaluation	Slightly bitter	Less bitter	Palatable
Zeta Potential (mV)	−29.4	−30.2	−31.2

All post-reconstitution evaluation parameters demonstrated that formulation RDDA3 was the optimized batch. Reconstitution time decreased from 85 to 45 seconds, indicating improved wettability and rapid dispersion with increased fenugreek mucilage concentration. Sedimentation volume ratio increased from 0.68 to 0.82, showing enhanced physical stability and formation of a loose, easily redispersible sediment. The number of strokes required for redispersion reduced from 85 to 55, confirming absence of hard caking and good suspendability. pH values remained within the acceptable oral range (6.2–6.6), ensuring stability and patient safety. Viscosity increased progressively (620–880 cP), contributing to reduced sedimentation without affecting pourability. Drug content ranged from 96.4% to 99.2%, confirming uniform drug distribution, while zeta potential values up to −31.2 mV indicated good electrostatic stability. Taste evaluation showed improved palatability in RDDA3. Overall, the results confirm that the optimized formulation exhibits superior stability, uniformity and patient acceptability.

ZETA POTENTIAL FORMULATION: 01

2026.01.23 16:01:17

HORIBA SZ-100 for Windows [Z Type] Ver2.60

HORIBA Scientific

SZ-100

Measurement Results

Date	:	23 January 2026 16:29:12
Measurement Type	:	Zeta Potential
Sample Name	:	Azithromycin Dry Syrup (F1
Temperature of Holder	:	25.0 °C
Dispersion Medium Viscosity	:	0.890 mPa-s
Conductivity	:	0.365 mS/cm
Electrode Voltage	:	3.3 V

Calculation Results

Peak No.	Zeta Potential	Electrophoretic Mobility
2	-29.4 mV	0.000215 cm2/Vs
3	-- mV	—
3	-- mV	—

Zeta Potential (Mean) : -29.4 mV

Electrophoretic Mobility Mean : -0.000215

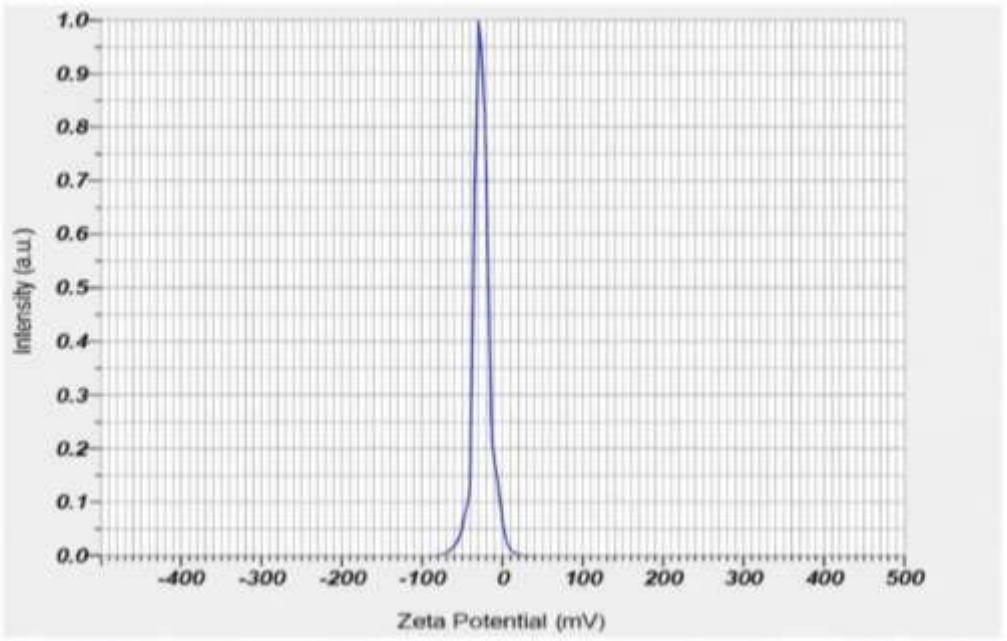

Figure no.7:zeta potential of formulation (1)

ZETA POTENTIAL FORMULATION:02

2026.01.23 16:10:20

HORIBA SZ-100 for Windows [Z Type] Ver2.60

HORIBA Scientific

SZ-100

Measurement Results

Date	: 23 January 2026 16:32:48
Measurement Type	: Zeta Potential
Sample Name	: Azithromycin Dry Syrup (F2)
Temperature of Holder	: 25.0 °C
Dispersion Medium Viscosity	: 0.890 mPa-s
Conductivity	: 0.365 mS/cm
Electrode Voltage	: 3.3 V

Calculation Results

Peak No.	Zeta Potential	Electrophoretic Mobility
2	-30.2 mV	0.000220 cm2/Vs
3	-- mV	—
3	-- —	—

Zeta Potential (Mean): : -30.2 mV
Electrophoretic Mobility Mean : -0.000220

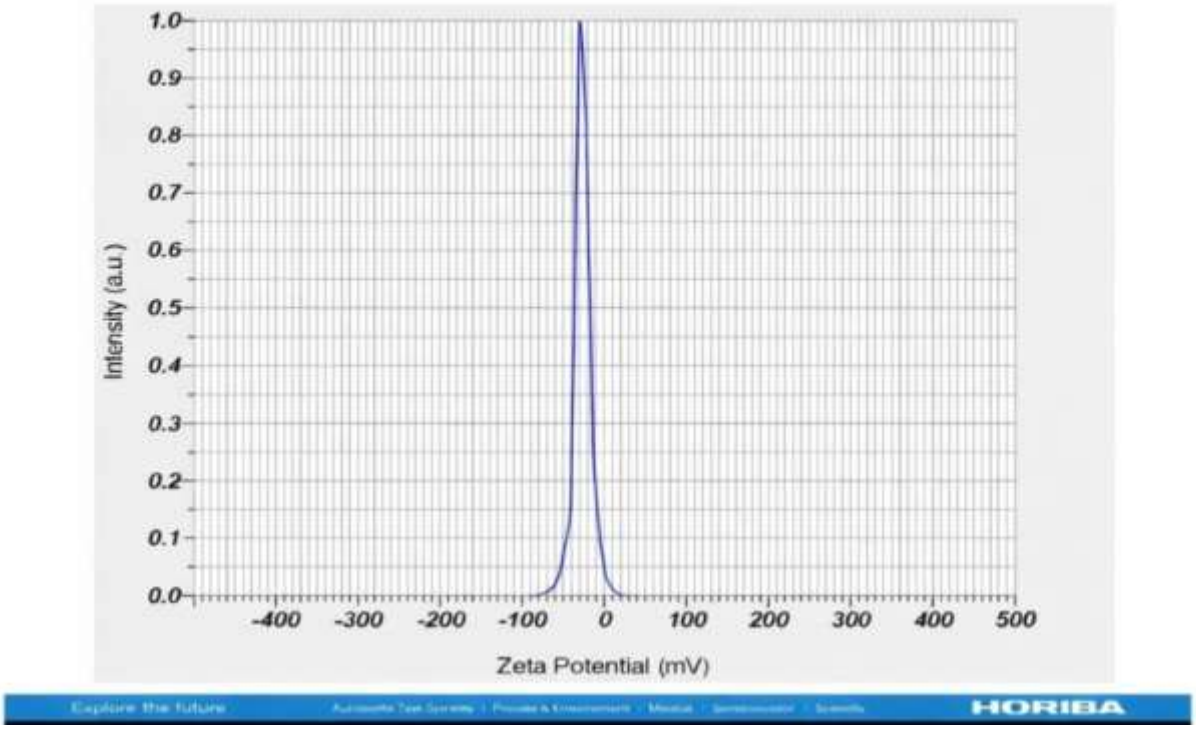

Figure no.8:zeta potential of formulation (2)

ZETA POTENTIAL FORMULATION :03

2026.01.23 15:31:42

HORIBA Scientific

HORIBA SZ-100 for Windows [Z Type] Ver2.60

SZ-100

Measurement Results

Date	: 23 January 2026 15:29:46
Measurement Type	: Zeta Potential
Sample Name	: Azithromycin + Fenugreek mucilage formulation F3
Temperature of the Holder	: 25.0 °C
Dispersion Medium Viscosity	: 0.892 mPa-s
Conductivity	: 0.374 mS/cm
Electrode Voltage	: 3.3 V

Calculation Results

Peak No.	Zeta Potential	Electrophoretic Mobility
1	-31.2 mV	−0.00255 cm²/Vs
2	— —	—002555

Zeta Potential (Mean)	: −31.2 mV
Electrophoretic Mobility Mean	: −0.00255 cm²/Vs

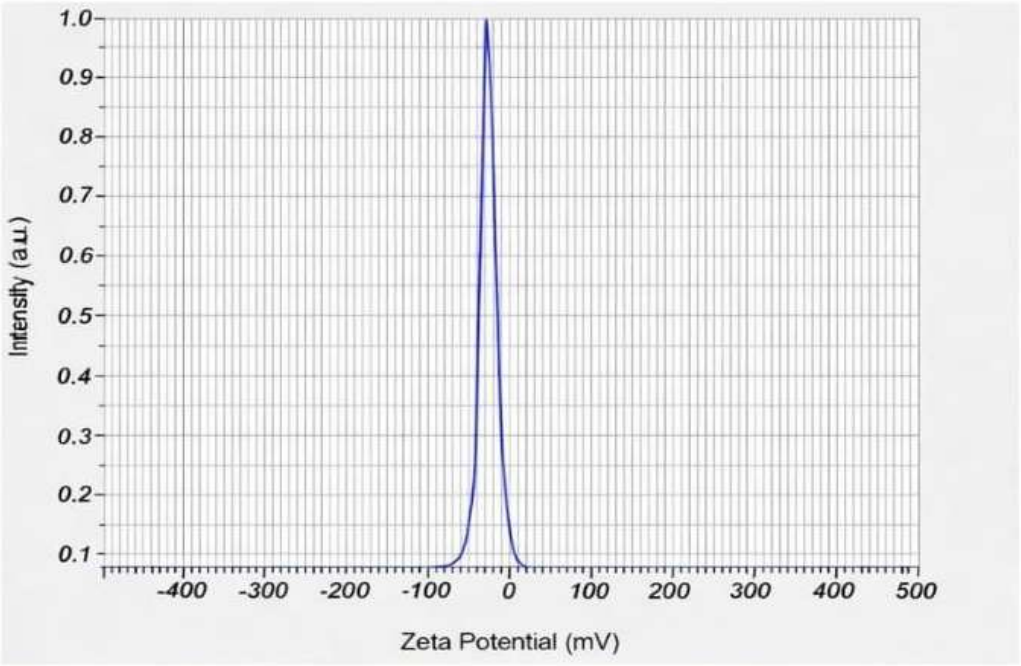

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Figure no.9:zeta potential of formulation (3)

DISSOLUTION TEST

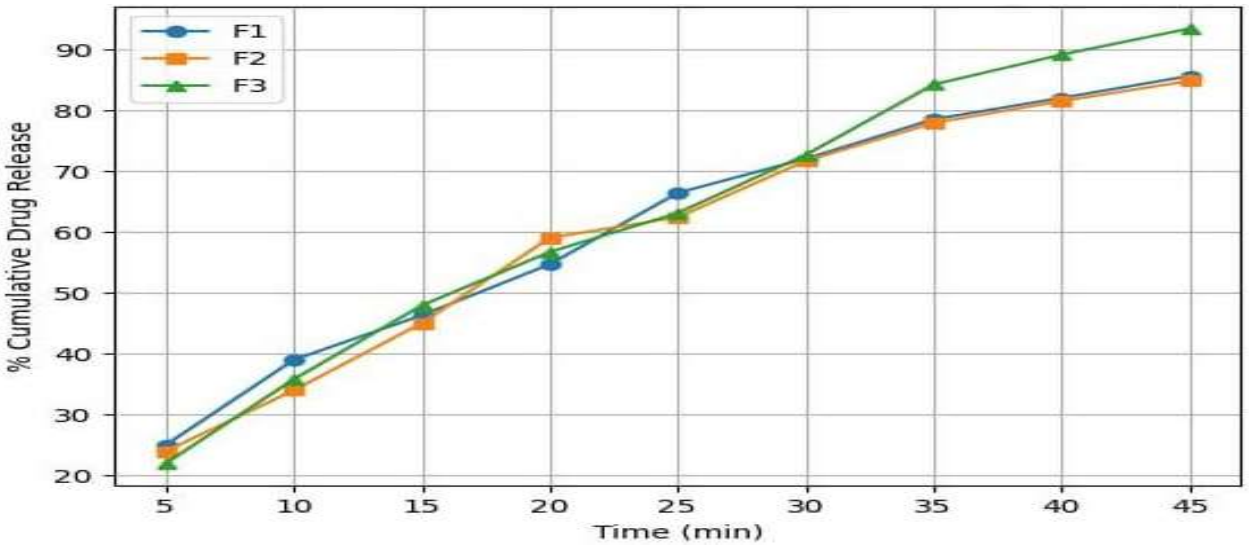

Figure no.10: drug release profile of Azithromycin dihydrate

Table no.10:Dissolution of formulation

Time	RDDA1(%drug release)	RDDA2(%drug release)	RDDA3(%drug release)
5	25.02%	24.00%	22.00%
10	39.00%	34.00%	35.80%
15	46.32%	45.01%	47.92%
20	54.68%	59.02%	56.70%
25	66.40%	62.41%	63.10%
30	72.00%	71.66%	72.64%
35	78.50%	77.90%	84.20%
40	82.00%	81.50%	89.10%
45	85.60%	84.80%	93.40%

The in-vitro drug release study showed a gradual increase in cumulative drug release for all formulations up to 45 minutes. Formulation RDDA1 and RDDA2 exhibited comparable and controlled release patterns, achieving 85.60% and 84.80% drug release at 45 minutes, respectively. In contrast, Formulation RDDA3 showed the highest drug release of 93.40% at 45 minutes, indicating improved dissolution behavior. The enhanced release from RDDA3 may be due to better formulation composition, resulting in superior drug dispersion and wettability. Overall, RDDA3 demonstrated better dissolution performance compared to RDDA1and RDDA2.

IN-VITRO DRUG RELEASE KINETICS

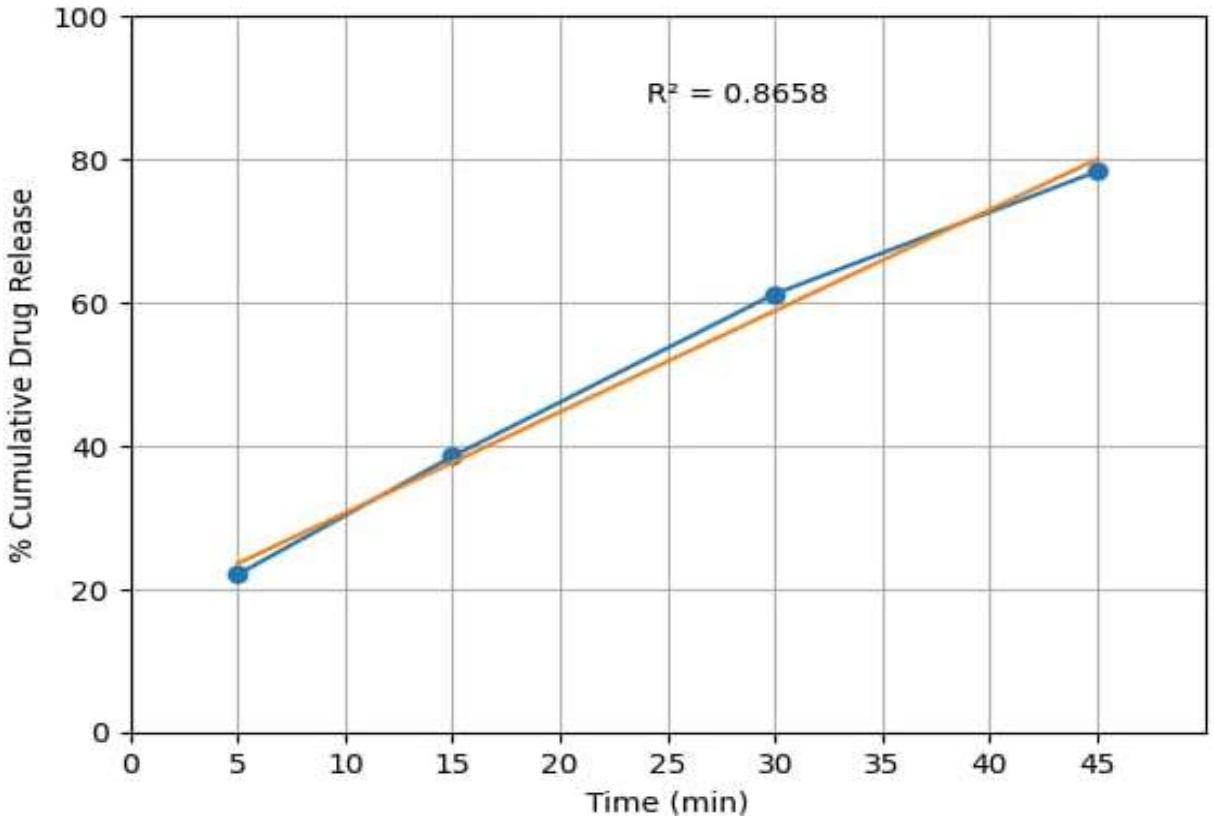

Figure no.11: zero order kinetics

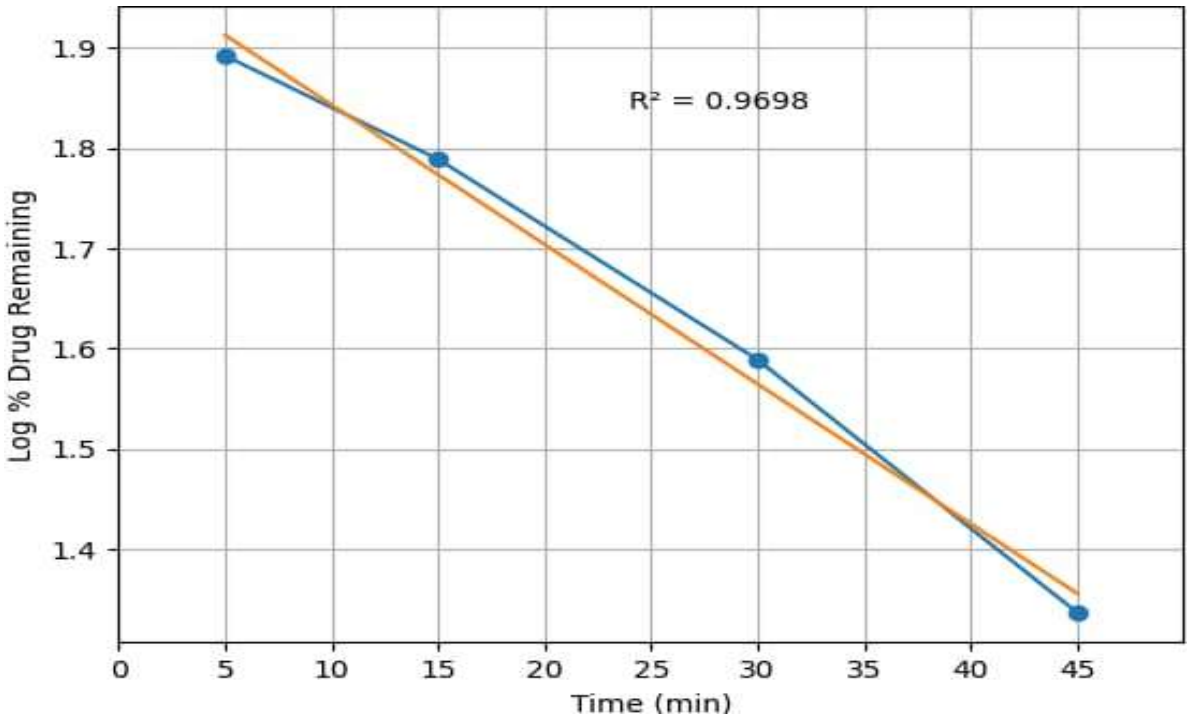

Figure no.12: first order kinetics

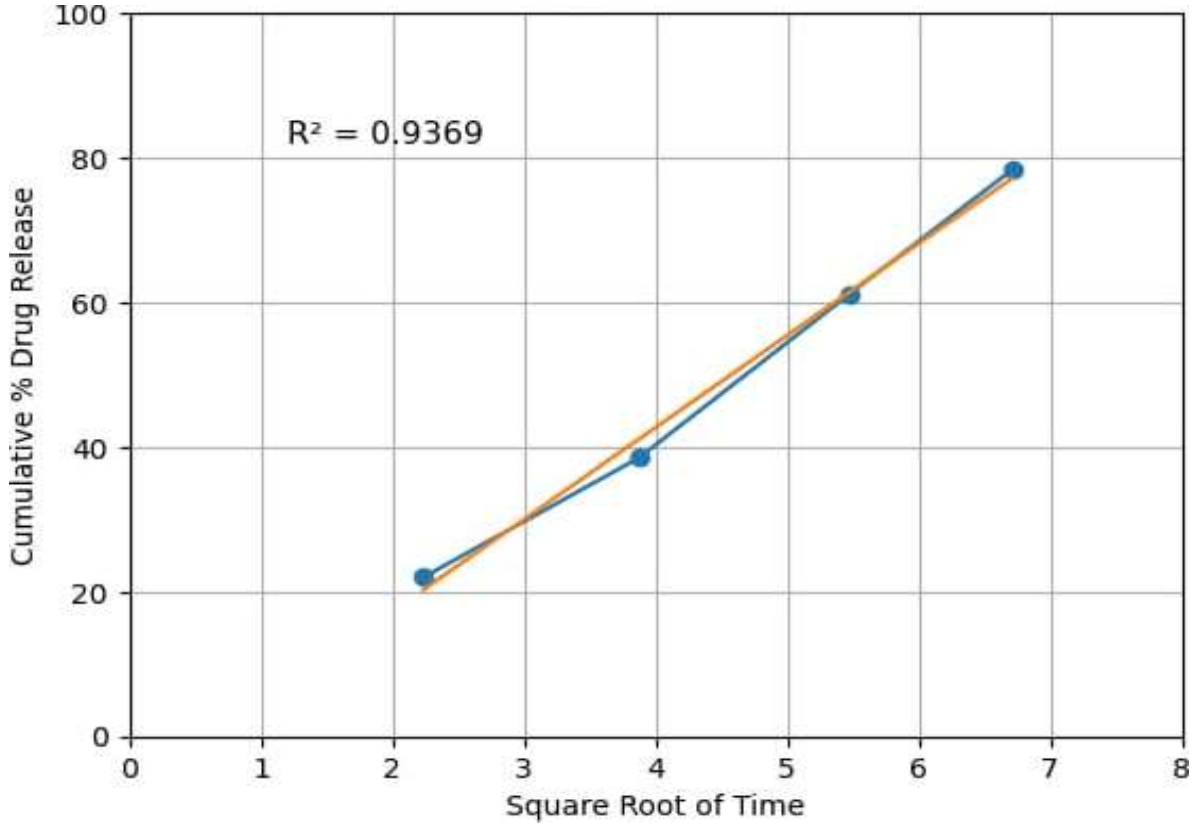

Figure no.13: Higuchi model

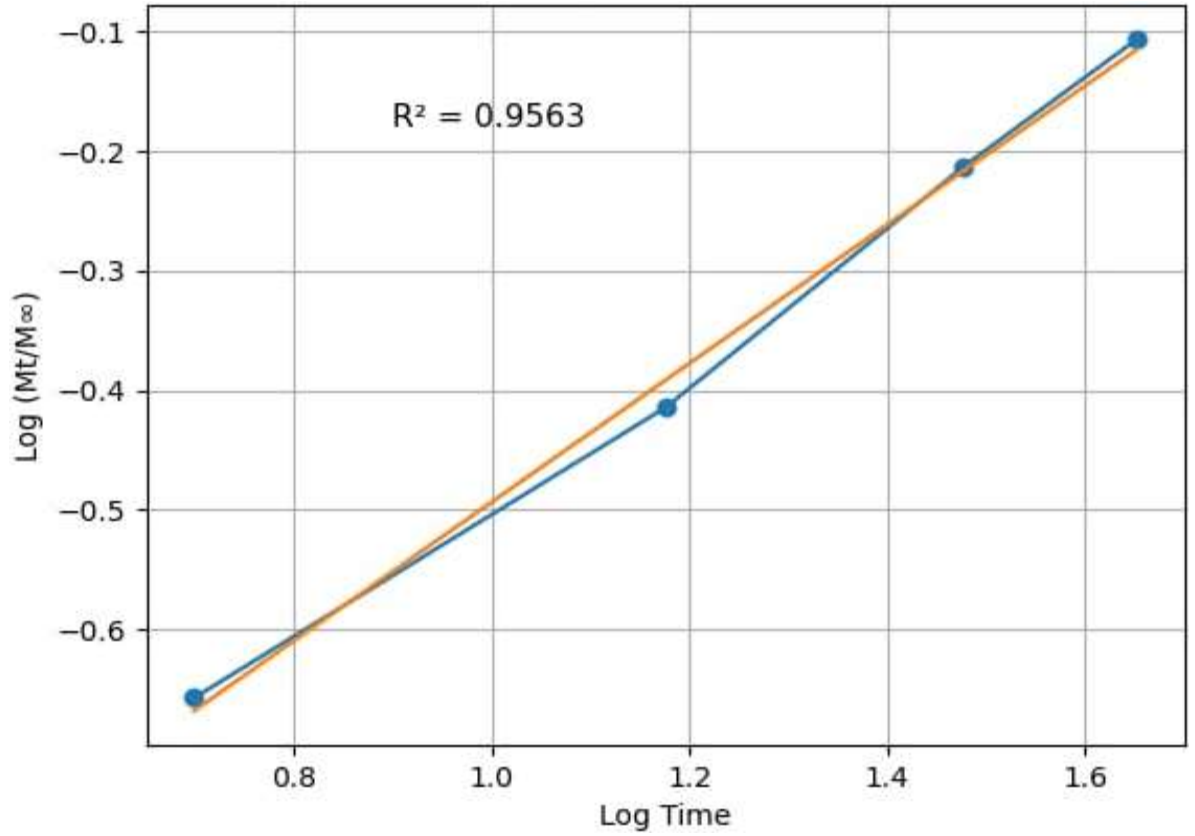

Figure no.14: Korsmeyer-peppas mode

The optimized formulation RDDA3 demonstrated a controlled and sustained drug release profile, achieving approximately 93–94% drug release within 45 minutes. The kinetic modeling of dissolution data was performed using Zero-order, First-order, Higuchi and Korsmeyer–Peppas models to elucidate the mechanism of drug release. Among the models evaluated, the First-order kinetic model showed the highest correlation coefficient (R^2 = 0.9698), indicating that the drug release rate is concentration-dependent. This suggests that as the amount of drug remaining in the formulation decreases, the release rate correspondingly declines.

The poor fit to the Zero-order model (R^2 = 0.8658) confirms that the formulation does not release the drug at a constant rate. The Higuchi model (R^2 = 0.9369) demonstrated good linearity, indicating that diffusion plays a significant role in the drug release mechanism. Since RDDA3 contains fenugreek mucilage as a natural suspending and matrix-forming agent, the polymer likely forms a hydrated gel barrier upon contact with dissolution medium. This gel layer regulates drug diffusion from the matrix into the surrounding medium. Further analysis using the Korsmeyer–Peppas model showed a good fit (R^2 = 0.9563) with an n value of 0.511. This value falls within the range of $0.45 < n < 0.89$, confirming a non-Fickian (anomalous) diffusion mechanism. This indicates that drug release is governed by a combined mechanism involving both diffusion through the polymer matrix and polymer swelling/relaxation. The contribution of fenugreek mucilage is critical here, as its swelling behavior enhances matrix integrity while simultaneously allowing controlled drug diffusion.Overall, formulation RDDA3 exhibits concentration-dependent, diffusion-controlled drug release with significant polymer relaxation influence. The optimized concentration of fenugreek mucilage effectively modulates drug release, providing sustained release characteristics. Therefore, RDDA3 can be considered the optimized formulation due to its desirable release kinetics, controlled dissolution profile and mechanistic consistency with non-Fickian transport behavior.

4.SUMMARY AND CONCLUSION

The present study was undertaken to formulate and evaluate a sugar-free reconstitutable dry syrup of Azithromycin dihydrate using fenugreek seed mucilage as a natural suspending agent. Azithromycin dihydrate, a widely prescribed macrolide antibiotic, suffers from poor aqueous solubility, bitter taste and instability in liquid dosage forms, making conventional syrups unsuitable, especially for pediatric and geriatric patients.

To overcome these limitations, a dry syrup approach was selected to enhance chemical stability, palatability and patient compliance. Fenugreek seed mucilage, rich in galactomannan polysaccharides, was successfully extracted and employed as a natural, biodegradable and non-toxic suspending agent, replacing commonly used synthetic polymers. The formulation was designed as sugar-free using stevia, making it suitable for diabetic and calorie-restricted patient.Preformulation studies such as organoleptic evaluation, solubility analysis, melting point determination, FTIR compatibility studies, UV spectroscopy, zeta potential and micromeritic evaluations confirmed the identity, purity and compatibility of Azithromycin dihydrate with fenugreek mucilage and other excipients. The powder blends showed acceptable bulk density, tapped density, Carr's index and angle of repose, indicating good flow properties suitable for dry syrup preparation.

After reconstitution, the formulations were evaluated for rheological behavior, sedimentation volume ratio, Redispersibility, pH, drug content and in-vitro dissolution studies. The results demonstrated that formulations containing fenugreek mucilage produced physically stable suspensions with good redispersibility, acceptable viscosity, uniform drug content and improved dissolution profile. Among the prepared batches, formulations with optimized mucilage concentration exhibited better suspension stability without excessive viscosity. Overall, the study concludes that fenugreek seed mucilage is an effective natural suspending agent and can be successfully used in the formulation of sugar-free reconstitutable dry syrups of Azithromycin dihydrate, offering a safe, economical, eco-friendly and patient-compliant alternative to synthetic excipients.

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