RESEARCH ARTICLE

Formulation And Evaluation of Quercetin Loaded Nanosponges of Abiraterone Acetate

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ABSTRACT

A novel idea in medicine delivery is the use of nanosponges. In the current research, an effort was made to create in-situ gel based on nanosponges that contained abiraterone acetate loaded with quercetin. The major purpose of nanosponges is to offer a prolonged release, lessen the negative effects of conventional dosage forms, and enhance the bioavailability of abiraterone acetate by using quercetin as a natural bioenhancer. Combining ethyl cellulose and eudragit in varying quantities, the quasi emulsion solvent diffusion technique was used to create nanosponges and quercetin as a natural bioenhancer. The formulation properties of the produced nanosponges were assessed. All batches of nanosponges had their manufacturing yield and trapping effectiveness assessed. Formulations F 03-P1 and F 07-P2 were found to be the optimum formulations based on results. Both F 03- P1 and F 07-P2 were used to create the gels G1 and G2. Viscosity, spreadability, drug content, and in-vitro tests showing 28.88% drug release after 24 hours all favored G2 as the optimal formulation. A gel base was created using the optimized formulation after it had been tested for scanning electron microscopy (SEM) analysis. Nanosponges containing gel had evaluated for different tests. According to the study, adding drugs to nanosponges can increase the rate of drug release, improve medication targeting at a particular spot, and hence lessen systemic toxicity.

Keywords: Abiraterone acetate, Nanosponges, Natural bioavailability enhancer.

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INTRODUCTION

Through their therapeutic aims, drug delivery technology has undoubtedly given pharmaceuticals a fresh interest. The main issue that researchers are currently dealing with is targeting medicine delivery. Targeted medication delivery, enhanced therapeutic efficacy, diminished adverse effects, and a more refined dosing protocol are expected to dominate the future of medicine's most promising field. One definition of targeted drug delivery is "the delivery of a therapeutically active pharmacological moiety to a specified site of action in an amount and time-dependent manner that minimizes exposure to non-target normal cellular linings and maximizes the drug's therapeutic index.[1]

Among American men, prostate cancer continues to be the second leading cause of cancer-related death.[2] The main treatment test used to slow the growth of prostate cancer and produce therapeutic results is androgen deprivation therapy.[3] Metastatic castration-resistant prostate cancer (mCRPC) and metastatic high-risk castration-sensitive prostate cancer (mCSPC) are two types of advanced prostate cancer that abiraterone acetate, the active pharmacological ingredient in the commercial tablet Zytiga®, has been licensed to treat. Log p value of abiraterone acetate (the ratio of octanol to water) is 5.12. This molecule is hydrophobic and is a tiny molecule. Abiraterone can be transformed from its inactive prodrug form, abiraterone acetate, by the enzyme esterase. The steroidogenic pathway requires the enzyme cytochrome P450 C17, which is inhibited selectively and irreversibly by abiraterone. As a result, prostatic tumor tissues produce less testosterone, which slows the growth of the tumor.[4-8]

Abiraterone acetate, a BCS class IV chemical, has limited solubility and permeability due to its unique structure.[9] When administered with food, abiraterone's absolute bioavailability is estimated to improve by a factor of 10 and by a factor of 17 compared to when it is administered while fasting.[10] The solubility of abiraterone and abiraterone acetate in the digestive fluids varies according to the fed state and the type of food consumed.[11] To lessen the likelihood of overexposure and major adverse effects, Zytiga® should be taken on an empty stomach at least an hour before or two hours after a meal. The higher daily doses of abiraterone acetate (1000 mg; four 250 mg tablets or two 500 mg tablets) are not cost-effective because

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of their poor absorption. There is a moderate two-fold increase in human bioavailability[12] when using the Yonsa® tablet dosage form, which contains abiraterone acetate particles with diameters between 200 and 800 nm. Utilizing pharmaceutical technology to improve solubility and bioavailability should be the primary focus of research into formulation design for BCS class IV drugs. Nanosponges have risen to prominence as a promising scientific field due to its potential use in controlled drug delivery. The delivery method for nanosponges significantly impacts the healthcare system since it allows for exact control of release rates or drug targeting to a particular bodily region. This research aims to apply nanosponges for the targeted and localized delivery of medicinal medicines/[13]

A three-dimensional network or scaffold is created by the sponge. Polyester in lengthy length makes up the backbone. The polymer is formed by dissolving it in a solution containing cross-linkers. The final product is a spherical particle with internal cavities that can store pharmaceutical compounds. Since polyester is biodegradable, it gradually breaks down inside of a living organism. As it disintegrates, it reliably releases the medicine inside. By adjusting the ratios of cross-linker to polymer, it is possible to create nanosponges with a specified size and drug release over time. To choose a molecule that is suitable for incorporation in to nanosponges, specific characteristics must be considered to ensure successful encapsulation. Nanosponges' biggest problem is that they can only store very small molecules.[14]

Nanosponges can be manufactured in a wide variety of dose forms, including oral, parenteral, topical, and inhalation. Small, solid particles called nanosponges have porous surfaces. The key benefits of these capsules or tablets are their extended release, lower toxicity, reduced overall dose, and increased patient compliance. These can be prepared into tablets or capsules by dispersing them in a matrix.[15] For local administration, they combine well with hydrogel.[16]

MATERIAL AND METHOD

Material

Abiraterone acetate, sodium alginate, quercetin, ethyl cellulose, Eudragit RS-100, Hydroxy propyl methyl cellulose, chitosan, cyclodextrin, pectin, Carbopol 971 P, propylene glycol, hydroxy ethyl cellulose, triethanolamine (2%), N-methyl-2-pyrrolidone.

Preformulation studies

The sample of drug loaded with bioenhancer and polymer was subjected to pre-formulation investigations, including ultraviolet (UV) spectroscopy research.

Saturated Solubility study

Using the Higuchi and Connors method, we conducted saturation solubility tests in triplicate. To test the drug's solubility, researchers put a surplus of the substance into 10 mL water vials and watched as it dissolved. The vials were shaken for 6 hours on a rotary shaker and then left alone for 24 hours to equilibrate. After 24 hours, filtered samples were diluted with distilled water and analyzed using a UV Spectrophotometer set to 235 nm.

Melting Point

A small amount was stored in a capillary tube sealed on one side and connected to the thermometer's mercury bulb. The thermometer was inserted into the thieles tube carrying the liquid paraffin so that its open, upper end was above the oil. Next, a hob was used to heat the Thieles tube's side arm to the melting point of the solid medication and the temperature at which it melted was recorded.

Drug - Excipient Compatibility Studies

KBr pellet approach with an FTIR spectrophotometer was used for the spectroscopic tests to determine the physical interaction between the medication, bioenhancer, and excipients. We then compare the spectrophotometer spectrum to the infrared range of the physical mixture. 400–4000 cm^{-1} is the scan range, and 4 cm^{-1} is the resolution (Tables 1 and 2).

Method

Quasi emulsion solvent diffusion method

The dispersed phase (Internal phase) consists of abiraterone acetate (API), Quercetin (Bioenhancer) and polymer dissolved in 20 mL of dichloromethane. Triethyl ether citrate (plasticizer) was added to the dispersed phase. Polyvinyl alcohol is dissolved in water to make up the aqueous phase (continuous phase). After stirring the aqueous phase at 1000 rpm for about 2 hours, the dispersed phase was added slowly while stirring. Filtration was used to harvest nanosponges, which were then dried in an oven at 400° for roughly 24 hours. Nanosponges are formed (Table 3), and then stored in a vacuum desiccator.[17]

Formulation of Nanosponges

During formulation and development of abiraterone acetate nanosponges, the following process variables to be studied

- Selection of polymer
- Ratio of drug and polymer

For nanosponges formulation, a suitable polymer shall be selected based on the outcome of the trials as shown in Table 1.

Formulation of Nanosponges by Quasi Emulsion Solvent Diffusion Technique

Formula for nanosponges formulation are shown in Table 3.

Characterization of Nanosponges Formulation

The formulated abiraterone acetate nanosponges were characterized for *in-vitro* drug release, loading efficiency, entrapment efficiency, particle size determination, SEM studies.[18-22]

Loading Efficiency

Spectrophotometric analysis accurately determined the total amount of drug present in nanosponges. In order to achieve a 1 g/mL concentration, 10 mg equivalent of abiraterone acetate-loaded nanosponges were placed in a beaker with (10 mL) of phosphate buffer and stirred for 30 minutes in a magnetic stirrer. Using a UV spectrophotometer, the absorbance was determined to be 235 nm.

Table 1: List of polymers used for trial

Drug	*Polymer*	*Ratio*	*Results observed*
Abiraterone Acetate	Ethyl cellulose	1:2	Two polymers, ethyl cellulose and eudragit RS-100, were chosen for creation of nanosponges after extensive testing and examination of a wide range of parameters.
	Eudragit RS-100	1:2	
	Hydroxy propyl methyl cellulose	1:2	
	Hydroxy ethyl cellulose	1:2	
	Sodium alginate	1:2	
	Chitosan	1:2	
	Cyclodextrin	1:2	
	Pectin	1:2	

Table 2: Polymer and drug ratio for nanosponges formulation

Code	*Drug*	*Polymer*	*Drug: Polymer ratio*
F1	Abiraterone Acetate	Polymer_I	1:0.5
F2		Polymer_I	1:1
F3		Polymer_I	1:1.5
F4		Polymer_I	1:2
F5		Polymer_II	1:0.5
F6		Polymer_II	1:1
F7		Polymer_II	1:1.5
F8		Polymer_II	1:2

(Polymer I = Eudragit RS-100, Polymer II = Ethyl cellulose)

Efficiency of loading (in percent) = 100 times (amount of drug loaded in nanosponges/total amount of drug utilised initially).

Entrapment Efficiency

Ultracentrifugation at 9,000 rpm for 30 minutes at 4°C was used to separate the entrapped drug from the nanosponges after 10 mg of abiraterone acetate was placed onto the nanosponges and the mixture was transferred to 10 mL of buffer. The free medication was carefully collected in the supernatant after centrifugation. The free drug content in the supernatant was determined by analyzing absorbance at 235 nm with a UV-spectrophotometer. Then, the following formula was used to get the entrapment efficiency (L):

L (%) = 100 x ((total drug quantity minus free drug amount) /total drug amount).

Particle size determination

At 25°C, abiraterone acetate loaded NS dispersal is measured for particle size and PDI via lively light spreading (PCS) with a Malvern Zeta sizer 3000 Nano S (Malvern instruments, UK). Each sample was irrigated down to the proper spreading strength with ultra-purified irrigation before it was filled to capacity. Throwaway-size cuvettes were used to collect the diluted NS dispersion, which was subsequently placed in the device's cuvette owner for analysis. Before taking a measurement, air bubbles are removed from the container.

Scanning Electron Microscopy (SEM)

SEM allows for intentional NS exterior formation. The batching's are doled out in a circular aluminum stub via double-sided adhesive tape, gold-plated in a HUS- 5GB vacuum evaporator, and put through their paces in a Hitachi S 3000N SEM with a rate power increase of 10 Kv and an exaggeration of 5000X.

***In-vitro* Release Studies**

The hemodialysis bag dispersion system appraised *in-vitro* release of abiraterone acetate from nanosponges. Studies of nanosponges were carried out using phosphate Buffer of pH 5.5. In 18 mg, corresponding abiraterone acetate nanosponges are unsettled in 10 mL of buffer pH 5.5 mixture in the hemodialysis container and preserved at both ends. The hemodialysis bag was engrossed in the lateral line cubicle with 100 ml buffer mix, which is enthused at 100 rpm and preserve 32 ± 2°C. The lateral line booth was enclosed to avert the disappearance of the distribution standard. All measurements must have been made with diffusion medium in place of the lateral line partition and the corresponding quantity. Up to 24 hours of sample taking is allowed. The samples were measured at 235 nm using a UV-spectrophotometer.

***In-situ* Gel Formulation of Prepared Nanosponges**

The gel- forming polymer was initially immersed in water for a period of 2 hours to facilitate gel formation. The soaked polymer was then agitated using a magnetic stirrer at a speed of 600 rpm to achieve a smooth dispersion. Triethanolamine was added at a concentration of 2% (v/v) to neutralize the

Table 3: Formula for nanosponges formulation

Formulation code	*Wt. of Drug (mg)*	*Wt. of bioenhancer (mg) (Quercetin)*	*Wt. of Polymer (mg)*	*Wt. of Polyvinyl Alcohol (mg)*
F 01_P1	250	100	50	200
F 02_P1	250	100	100	200
F 03_P1	250	100	150	200
F 04_P1	250	100	200	200
F 05_P2	250	100	50	200
F 06_P2	250	100	100	200
F 07_P2	250	100	150	200
F 08_P2	250	100	200	200

pH. Subsequently, the previously optimized nanosponge formulation was incorporated into the gel. Additionally, a methanolic solution of propylene glycol added as a permeation enhancer. Table 4 lists the individual ingredients that go into making the nanosponge gel. Based on the nanosponge formulation's characterization results, F 03_P1 and F 07_P2 were chosen for the development of in-situ gel formulations (Table 4).

Characterization of Insitu Gel Formulation-

Visual appearance

The formulated gel loaded with nanosponges was inspected for their color and appearance. The gel loaded batches were appearing transparent white with uniform distributed microsponges, as shown in Table 4 with no lumps and air bubbles in the gel. Formed air bubbles were removed by keeping the gel undisturbed for overnight and sonicated.

Clarity

Clarity of the prepared abiraterone acetate-loaded gel was checked visually against a white screen background.

pH

After incorporating all of the components, the in-situ gelling system's pH was measured.

Viscosity

The Brookfield viscometer gave a firm reading for the viscosity. The stickiness of the research was computed using spindle no. S64 at a best speed of 0.6 rpm in the recent revision.

Drug content

Soften precisely weighed measure of gel corresponding to 9 mg of the pills in a glass hold 10 mL of ethanol, stir the solution for 30 minutes, ultracentrifuge in High-speed cooling ultracentrifuge, and make upto 10 mL with phosphate buffer pH 5.5 to confirm the drug content of the ready gel. Using a UV-visible spectrophotometer, we measured the concentration in comparison to a blank reading.

In vitro drug release study

A hemodialysis bag was used on purpose for an in-vitro medication release investigation. The 18 mg of NS gel should be placed in a hemodialysis bag that is 8 cm in length and 3 cm in breath and secured on both ends with thread. The booth for donors to sign in was here. The bag was then placed in a lateral line cubby made from a cup containing 100 cc of phosphate buffer pH 5.5. An attractive disruptor maintained a 37°+2°C temperature in the lateral line middle and enlivened the midway at a haste of 100 rpm.

Table 4: Formulation of nanosponges gel

Sr. No.	*Ingredients*	*Polymer I (F 03_P1)*	*Polymer II (F 07_P2)*
1	Formulated nanosponges	80 mg	80 mg
2	Carbopol 971 P	150 mg	150 mg
3	Distilled water	10 ml	10 ml
4	Propylene glycol	0.5 ml	0.5 ml
5	Triethanolamine (2%)	1 ml	1 ml
6	N-methyl-2-pyrrolidone	0.2 ml	0.2 ml

(Polymer I = Eudragit RS-100, Polymer II = Ethyl Cellulose)

RESULT AND DISCUSSION

Preformulation Results

Saturation solubility study

Abiraterone acetate's saturation solubility in distilled water was calculated using the Higuchi and Conners method. With a solubility of 0.097 and 0.032 mg/mL, abiraterone acetate has a low aqueous solubility. The outcomes are consistent with what has been reported before.[23,24]

Melting point

Abiraterone acetate's melting point was measured to be 144.66°C, within the melting point range reported in the literature (144–145°C). This means the medicine is 100% pure (Table 5).

Maximum wavelength (λ_{max})

The abiraterone acetate solution was scanned between 200 and 400 nm in spectral mode. The highest wavelength of absorption was determined to be 235 nm (Figure 1).

Standard calibration curve

Correctly weighed 100 mg of Abiraterone Acetate in a 100 mL calibrated flask. Then 20 mL of methanol was incorporated gradually to dissolve the drug. It was then produced until 100 mL volume using methanol and made stock of 1000 µg/mL concentration.

A further 2.5 mL pulled in a 100 mL calibrated flask and produced until 100 mL with methanol at 25 µg/mL. Similarly, 5, 7.5, 10, 15, 20, 25 mL pulled to 100 mL calibrated flask and produced with methanol to give 50, 75, 100, 150, 200, 250 µg/mL solutions (Tables 6 and 7 and Figure 2).

Table 5: Melting point of abiraterone acetate

Sr. No.	*Obtained range (°C)*	*Mean value (°C)*	*Reference value*
1.	146		
2.	145	144.66	144–145
3.	143		

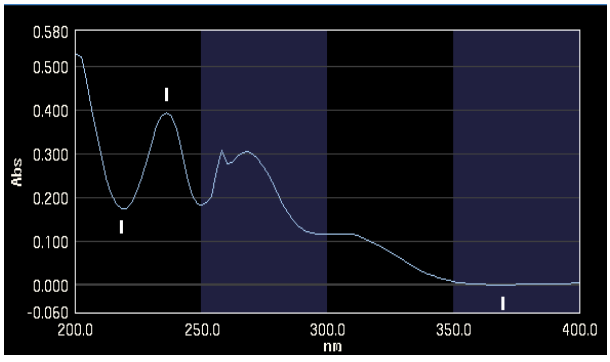

Figure 1: Maximum wavelength of abiraterone acetate (235 nm)

Table 6: Different concentration and absorbance

Conc.(µg/ml)	*Absorbance*
25	0.125
50	0.261
75	0.359
100	0.581
150	0.825
200	1.124
250	1.398

Table 7: Parameters found in the calibration curve

Parameters	*Drug (AB)*
Wavelength (nm)	235 nm
Linearity range (µg/mL)	25-250 µg/mL
Regression equation	y = 0.0056x
Regression Coefficient (R^2)	0.9964

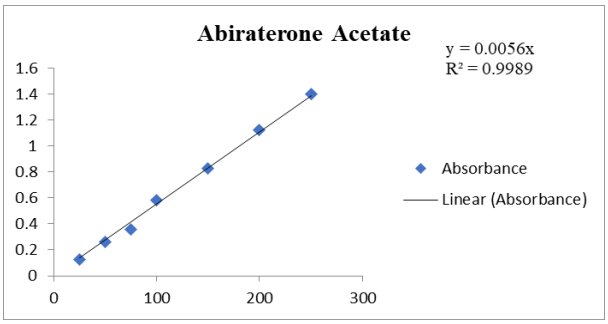

Figure 2: Calibration curve of abiraterone acetate (235 nm)

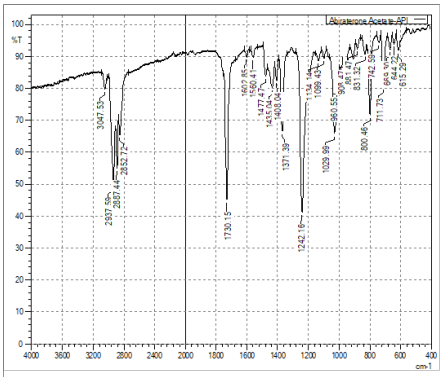

Figure 3: Spectrum of infrared spectroscopy (Abiraterone Acetate)

Drug and Excipient Compatibility Study

Drug excipient compatibility study was carried out using standard procedures.

The IR Spectrum of test sample (Abiraterone Acetate) was found to be concordant with that of the standard spectrum (Table 8 and Figures 3 and 3A).

The characteristic FTIR spectrum is seen in pure quercetin, with peaks around 3400 to 3230 cm^{-1} and 1365 cm^{-1} for the phenolic group's O-H stretching and O-H bending,

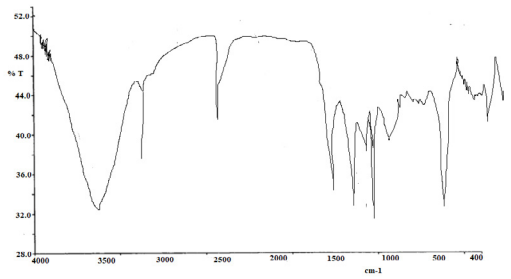

Figure 3A: FTIR Spectra of quercetin

Table 8: IR absorption bands of drug

Frequency (cm^{-1})	*Functional groups*
OH (Stretching)	3047.53
Alkane (CH3,CH2 and CH-Stretching)	2937.59
C-O (Stretching)	2335.80
C=O (Stretching)	1730.15
C-O-C Ether (Stretching)	1560.41
Aliphatic C-C (Stretching)	1438.90
Aliphatic C-H (Bending)	1371.39
Ester C-O (Stretching)	1242.16
-C-H (Bending)	711.73

Figure 4: Formulated nanosponges by quasi emulsion solvent diffusion technique

Table 9: Drug content and loading efficiency of abiraterone acetate nanosponges

Formulation code	*Drug Content (%)*	*Loading Efficiency (% w/v)*
F 01_P1	93.31 ± 0.633	98.43
F 02_P1	91.52 ± 0.109	98.16
F 03_P1	90.54 ± 0.164	98.97
F 04_P1	92.42 ± 1.230	98.72
F 05_P2	90.31 ± 0.344	95.16
F 06_P2	88.42 ± 0.512	91.45
F 07_P2	92.16 ± 0.514	99.15
F 08_P2	89.46 ± 0.421	94.75

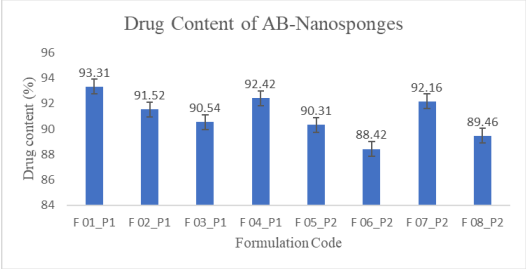

Figure 5: %Drug content of abiraterone acetate nanosponges

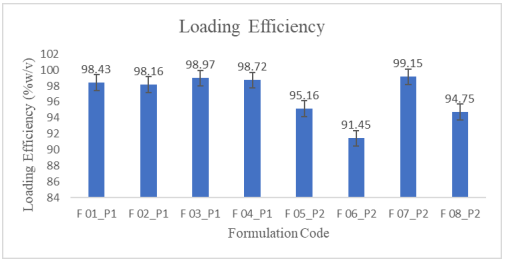

Figure 6: Loading efficiency of abiraterone acetate nanosponges

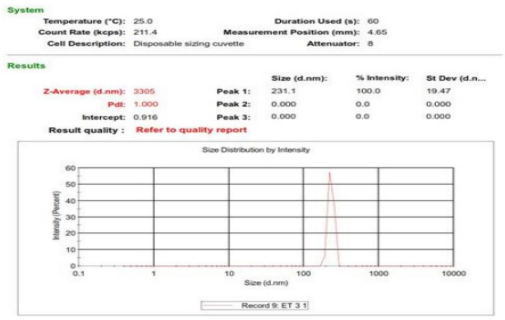

Figure 7: Particle size distribution by malvern zeta sizer (F 03_P1)

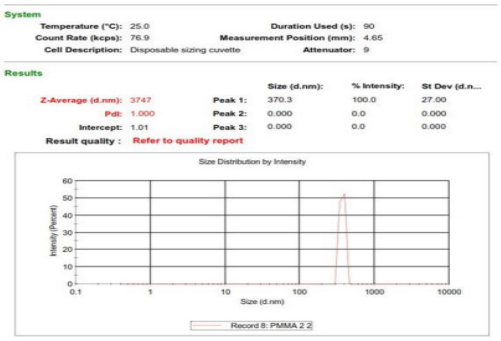

Figure 8: Particle size distribution by malvern zeta sizer (F 07_P2)

respectively. Bands at 1615, 1560 and 1513 cm^{-1} indicate the C=C aromatic ring stretch, whereas the C=O aryl ketonic stretch occupy 1664 cm^{-1}.

The results showed a loading efficiency of 91.45 to 99.15 percent. F 03_P1 and F 07_P2 had a loading efficiency of 99.15 and 98.97, respectively (Table 9, Figures 4-6).

Particle size determination

The polydispersity index for Abiraterone Acetate-loaded N.S. was determined to be 1, and the average particle size was 231.1 nm (Figure 7).

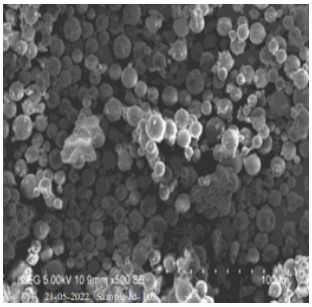

Figure 9: SEM image of optimized formulation of microsponges (F 03_P1)

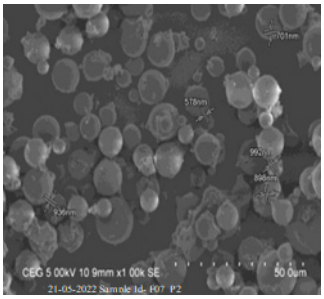

Figure 10: SEM image of optimized formulation of microsponges (F 07_P2)

Table 10: *In-vitro* drug release of api and abiraterone acetate nanosponges

Time in hours	*Drug API*	*F 01_P1*	*F 02_P1*	*F 03_P1*	*F 04_P1*
0	0	0	0	0	0
1	0.61	1.7	1.74	2.84	2.07
2	0.84	3.49	2.54	5.06	3.57
3	0.66	4.45	3.61	8.41	5.29
4	0.69	5.68	4.87	10.69	6.32
5	1	6.82	4.97	13.06	7.71
6	1.17	7.71	5.71	14.55	8.51
7	1.31	9.28	6.95	16.75	10.04
8	1.58	11.12	8.47	18.61	10.66
9	1.74	12.38	9.07	19.71	11.09
10	1.8	14.03	9.8	22.51	11.61
11	1.91	16.84	10.79	24.44	12.81
23	2	17.97	17.52	31.92	17.8
24	2.54	20.11	23.3	36.28	20.46

PDI was found to be 1 and the average particle size of the NS loaded with abiraterone acetate was 370.3 nm (Figure 8).

Scanning Electron Microscopy (SEM)

SEM image of optimized formulation of microsponges (F 03_P1 and F 07_P2) as shown in Figure 9 and 10.

In-vitro release studies

The result showed that the group F 03_P1 and F 07_P2 showed sustained drug release (Figures 9 to 12 and Tables 10 and 11).

Table 11: *In-vitro* drug release of API and abiraterone acetate nanosponges

Time in hours	*Drug API*	*F 05_P2*	*F 06_P2*	*F 07_P2*	*F 08_P2*
0	0	0	0	0	0
1	0.61	1.23	1.27	4.14	1.63
2	0.66	2.47	2	7.3	2.94
3	0.84	3.8	2.81	10.16	4.06
4	1	5.75	3.63	14.13	5.24
5	1.12	6.65	4.96	15.94	6.47
6	1.31	7.72	5.25	18.69	7.67
7	1.58	9.85	6.15	20.72	8.65
8	1.74	10.38	7.16	23.2	9.35
9	1.8	12.23	7.49	27.06	10.53
10	1.91	12.96	8.54	29.16	11.49
11	2	13.79	9.0	35.58	12.47
23	2.54	20.02	14.5	41.45	17.61
24	2.63	22.71	15.35	45.66	19.11

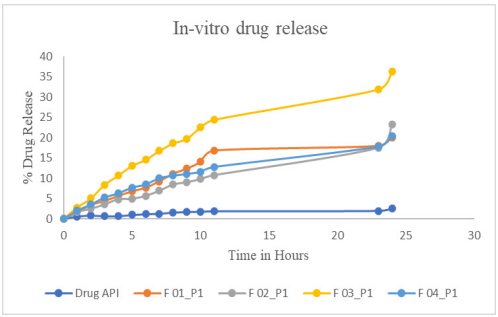

Figure 11: *In-vitro* drug release

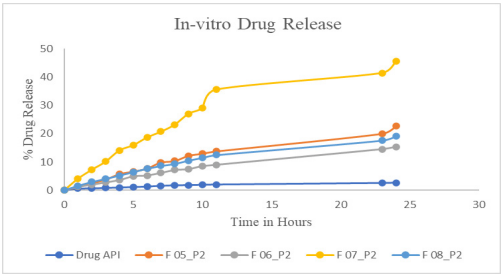

Figure 12: *In-vitro* drug release of API and abiraterone acetate nanosponges

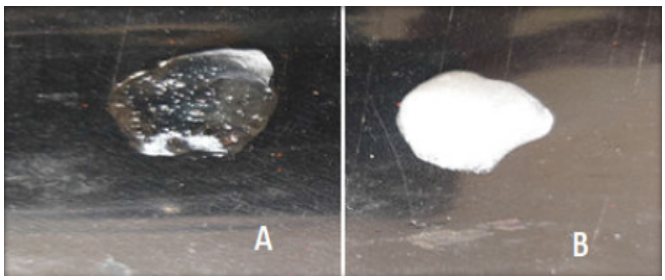

Figure 13: (A) Gel, (B) Gel loaded with formulated nanosponges

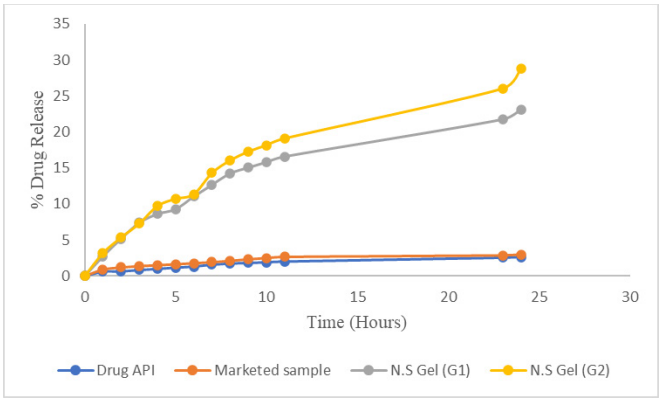

Figure 14: *In-vitro* drug release of API, marketed sample and abiraterone acetate NS gel (G1 and G2)

Table 12: Physical appearance, viscosity, drug content, pH and drug release of formulation G1and G2

Code	*Physical Appearance*	*%Drug content*	*Viscosity (cps)*	*pH*	*%Drug release*
G1	Good	91.10	2.939×10^6	4.89	25.15
G2	Good	94.55	2.853×10^6	4.92	28.88

Table 13: *In-vitro* drug release of Drug API, marketed sample (Abirapro®) and abiraterone acetate nanosponges gel (G1 and G2)

Time in Hours	*Drug API*	*Marketed sample*	*NS Gel (G1)*	*NS Gel (G2)*
0	0	0	0	0
1	0.61	0.9	2.73	3.18
2	0.66	1.2	5.18	5.36
3	0.84	1.39	7.39	7.28
4	1	1.51	8.62	9.73
5	1.17	1.64	9.28	10.73
6	1.31	1.79	11.03	11.37
7	1.58	1.92	12.66	14.3
8	1.74	2.11	14.24	16.06
9	1.8	2.33	15.05	17.28
10	1.91	2.5	15.81	18.17
11	2	2.66	16.59	19.12
23	2.54	2.87	21.75	26.04
24	2.63	3.01	23.15	28.86

In-situ Gel Formulation

NS gel (G1 and G2) release was 23.15 and 28.88%, respectively, when compared with a commercially available sample of a tablet containing abiraterone acetate (Figures 13, 14) (Tables 12 and 13).

Stability Study

The findings of the stability studies showed that the prepared groups maintained a consistent level of drug content throughout the whole testing period.

CONCLUSION

In this work, researchers reported a novel method of employing quercetin as a bioenhancer to augment the bioavailability of the medication abiraterone acetate, allowing for its continued administration to the treated area. Nanosponges were fabricated using the Quasi Emulsion Solvent Diffusion method by adding ethyl cellulose and eudragit at varying quantities. FTIR analysis depicted that the medication, bioenhancer, and excipients were all compatible. Formulations F 03 _P1 and F 07 _P2 were deemed superior through their efficient drug entrapment, drug content, and drug release. Gels G1 and G2 were made with the formulas F 03 P1 and F 07 P2, respectively. G2 was chosen as the finest preparation by its viscosity, spreadability, drug content, and *in-vitro* results, demonstrating a drug release of 28.88% at the 24-hour mark. The optimization process yielded a stable G2 formulation, as determined by the stability study.

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