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Advances in Bioresearch

ORIGINAL ARTICLE

Formulation and *In Vitro* Evaluation of Bilayer Tablets of Bicalutamide and Curcumin

Shilpa P. Chaudhari, Dhanaji S. Suryavanshi*
Dr. D. Y. Patil College of Pharmacy, Akurdi, Pune- 411 044, Maharashtra, India
Address for Correspondence: Dhanaji Suryavanshi [dhanajipharma@gmail.com]

ABSTRACT
Prostate cancer is often described as a disease of the developed world, a fact confirmed by its higher incidence rates. However, of the 307,471 deaths from prostate cancer reported in 2012, over 50% occurred outside of the United States and Europe. The present work involves the formulation development, optimization and In-vitro evaluation of bilayer tablet containing Curcumin (CCM) in the immediate release layer and bicalutamide (BCT) in the sustained release layer, using sodium starch glycolate as a super disintegrant for the immediate release layer and the hydrophilic matrix HPMC-K100 are used in the sustained release layer. Bilayer tablet showed as initial burst effect to provide dose of immediate release layer Curcumin to control the acid secretion level and the sustained release of bicalutamide for 24 hours. The prepared bilayer tablet was evaluated for their precompression parameters, physical characteristics like hardness, friability, uniformity of weight, uniformity of drug content, swelling index and In-vitro drug release. The release of the Curcumin from the immediate release layer was found to be 98.87 ± 0.15% in 45 minutes. The release of bicalutamide for the sustained release layer was found to be 97.32% in 24 hours. Curcumin potentiate the effect of bicalutamide. Hence the bilayer tablets of Curcumin and bicalutamide were used to improve patient compliance towards the effective management of Prostate cancer.
Keywords: *Prostate cancer, Curcumin, Bicalutamide, Bilayer Tablets*

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INTRODUCTION

Prostate cancer is the most common cancer in males worldwide. The incidence and mortality rates for prostate cancer vary widely between population groups around the world [1]. Prostate cancer is the second most diagnosed type of cancer and the fifth leading cause of death in the worldwide male population, with mortality rates increasing from 150,000 to 250,000 between 1990 and 2010. In 2018, 1,276,106 new cases were diagnosed and 358,989 deaths were reported [2]. The epidemiology of the disease varies amongst different countries; it is most commonly present in European, Australian, North American, and African American men, whereas, in Asia, prostate cancer has a lower prevalence. The risk factors for prostate cancer include family history, obesity, old age, and ethnicity [3-5]. As the second most common cause of death amongst men in the United States, prostate cancer is a type of cancer that is known to develop and originate in the prostate gland. Prostate cancer is most commonly seen in patients over the age of 66 years, however, in the presence of predisposing risk factors, may occur as early as in the late 40s [6].

Curcumin or diferuloylmethane, a polyphenolic molecule extracted from the rhizome of the plant *Curcuma longa*, is a promising chemopreventive compound. This natural compound is a yellow spice used as curry ingredient and is used since centuries in Ayurvedic, Chinese, and Hindu medicine systems as a potent anti-inflammatory agent. It is under investigation since several years for its major mechanisms of action and functions. The reported studies revealed that Curcumin possesses anti-oxidant, anti-inflammatory, anti-proliferative, and anti-angiogenic properties against several cancer cell types and also demonstrates anti-microbial activities. Nowadays, Curcumin is under clinical trials mainly for cancer and related diseases [7-9].

Bicalutamide is a nonsteroidal pure antiandrogen given at a dosage of 150mg once daily as monotherapy for the treatment of early (localized or locally advanced) nonmetastatic prostate cancer. Bicalutamide is a racemate and its antiandrogenic activity resides almost exclusively in the (R)-enantiomer, with little, if any, activity in the (S)-enantiomer. (R)-Bicalutamide is slowly and saturably absorbed, but absorption is unaffected by food. It has a long plasma elimination half-life (1 week) and accumulates about 10-fold in plasma during daily administration. Bicalutamide (Casodex) is a nonsteroidal antiandrogen that competitively inhibits the action of androgens by binding to the androgen receptor. Bicalutamide increases both testosterone and estradiol levels, and the estradiol levels approximate the low-normal levels of a premenopausal woman [10-13].

Bilayer tableting technology has gained popularity in recent times, as bilayer tablets offer several advantages over conventional tablets. Usually conventional dosage form produce wide ranging fluctuation in drug concentration in the blood stream and tissues with consequent undesirable toxicity and poor efficiency. This factor such as repetitive dosing and unpredictable absorption led to the concept of controlled drug delivery systems. The bilayer tablet concept has long been utilized to formulate biphasic release of drugs. Such a bilayer tablet contains a first release layer and a sustain release layer. The first releasing layer leads to rapid release of the drug, so as to reach high serum concentration in a short period of time that is called as loading dose. The sustain release layer of the bilayer tablet releases the drug for the prolonged period of time to maintain the effective concentration of drug within the therapeutic index [14-16].

Combination therapy, a treatment modality that combines two or more therapeutic agents, is a cornerstone of cancer therapy. The amalgamation of anti-cancer drugs enhances efficacy compared to the mono-therapy approach because it targets key pathways in a characteristically synergistic or an additive manner. This approach potentially reduces drug resistance, while simultaneously providing therapeutic anti-cancer benefits, such as reducing tumour growth and metastatic potential, arresting mitotically active cells, reducing cancer stem cell populations, and inducing apoptosis [17-19].

The aim of present research work was undertaken to formulate bilayer tablets of Curcumin and bicalutamide through its incorporation of an oral dosage form that is able to release Curcumin immediately as well as sustained release of bicalutamide for 24 hrs to enhance the oral bioavailability of bicalutamide. The main objective of this work was formulation of bilayer tablets composed of two different classes of drugs by using a simple and easy-to-scale-up formulation strategy.

MATERIAL AND METHODS

Bicalutamide were obtained as gift samples from Cipla ltd. Goa, India. Curcumin and other ingredients were obtained as a gift sample Helax health pharmaceuticals, Mumbai (India). Xanthan gum and HPMC-K100 were gifted by Aurobindo Pharma, Hyderabad, India. Sodium starch glycolate, and Lactose monohydrate, were procured from SD Fine Chemicals, Mumbai, India. Sodium starch glycolate, and Polyvinyl pyrolidone were gifted from Medibios pharmaceuticals, Bhoisar, Mumbai (India),

- **Compatibility studies of drug and polymers:**

Fourier transform infrared spectrometry (FTIR)

Approximately 300mg of KBr was weighed and grind to a fine powder, and then approximately 1mg of the Pure drug/combination of drug-excipients was added and grinded well to mix the sample with the KBr and then press this KBr mixer and made a palate by using IR press at the pressure of 8-tons [12].

Differential Scanning Calorimetry (DSC)

The DSC exploration confirmed physical stature of inherent medication esoteric the nanoparticles. The sample remains placed and wrapped typical aluminum pan and was perused between 25 °C to 300 °C with a heating rate of 10°C/minute beneath nitrogen atmosphere. A blank aluminum pan served as reference [13].

- **Preparation and optimization of bilayer tablets:**

Preparation of Immediate Release Curcumin Granules

To improve the onset of action the immediate granules of Curcumin were prepared by wet granulation technique. Curcumin and other excipients like Xanthan gum, Sodium starch glycolate and Dicalcium phosphate were accurately weighed and sifted through sieve #40 and mixed in a polybag. The sifted powders were thoroughly mixed for approximately 5 min and again passed through sieve #40 to get uniform particle size. Magnesium stearate was added into the powder mixture for lubrication after passing through sieve #40. The granules were compressed by 10 station compression machines. Composition of tablets is mentioned in Table 1. The immediate release tablet of Curcumin was formulated and optimized. The optimized formulation was used for the final bilayer tablets.

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Preparation of Sustained Release Bicalutamide solid dispersions Tablets

Firstly Bicalutamide solid dispersions was prepared by Solvent evaporation method, in which polymers (PEG-20000) were dissolved completely in Ethanol in different ratio in a beaker. Bicalutamide was dispersed in the solution in Drug: polymer ratio of 1:4. The resulting solution was kept on the water bath (at 60 ± 0.5^0C) to remove the solvent from resulting mixture. The obtained mass was dried. The resultant mass was pulverized using a glass mortar and pestle. The pulverized mass was sifted through # 60, weighed and transferred to the glass vials. In second step, Sustained release layer of Bicalutamide solid dispersions was prepared by wet granulation technique by adding Lactose monohydrate, Sodium starch glycolate, polyvinyl pyrolidone and Xanthan gum. Required quantities of Bicalutamide solid dispersions and other excipients were weighed accurately and were sifted through sieve #40 and were mixed thoroughly and a sufficient volume of binding agent was added slowly to get cohesive mass. Then mass was passed through sieve #20 to obtain the granules. Next the granules were dried at 50°C in a hot air oven until dry the dried granules were lubricated uniformly with magnesium stearate; then talc was added and mixed properly. The above granules were compressed into tablets by 10-station tablet compression machine (Mini Press I, Karnavati, Gujarat, India) using 9 mm punch [15-18].

Preparation of Bilayer Tablets [19]

Formulation of bilayer tablet Optimized formulation N-2 of Instant release layer (Curcumin) and optimized formulation of NA-4 (Bicalutamide) for control release used for formulation of Bi-layer tablet. Optimized immediate layer of Curcumin was prepared by wet granulation method. Optimized sustained release layer of Bicalutamide was prepared by wet granulation method. First, Immediate release Curcumin layer was placed in the lower die cavity and punched with low compression force. Then the Sustained release Bicalutamide solid dispersions tablets was placed in the die cavity then again immediate release Curcumin layer was placed in the Upper die cavity and allowed for punching with optimum hardness of 6–8 kg/cm^2 to form bilayer tablets. Compression was made by using 10 mm punches (Mini Press I, Karnavati, Gujarat, India). The total weight of each bilayer tablet was adjusted to 400 mg, containing 100 mg of Curcumin in fast-release layer and 50 mg of bicalutamide in sustained release layer. Prepared bilayer tablets were evaluated for various post-compression parameters and *in vitro* dissolution studies [16-17].

- **Characterization parameters**

Appearance:

The appearance was acknowledged visually through proving the colour variance.

Hardness:

The hardness of a tablet is indicative of its tensile strength and is measured in terms of load/pressure required to crush it when placed on its edge. A number of handy hardness testers such as the Mosanto type or Pfizer type are currently in use. Hardness of about 5 kg is considered to be a minimum for uncoated tablets for mechanical stability. The hardness is a function of physical properties of granules such as hardness and deformation under load, binders and above all the compressional force. The hardness has an influence on disintegration and dissolution times and is, as such, a factor that may affect bioavailability.

Thickness:

A Mitutoyo Digital Vernier calliper stood adopted to regulate the thickness of ten arbitrarily designated tablets [18]. The thickness of individual tablets may be measured with a micrometer, which permits accurate measurement and provide information on the variation between tablets. The thickness should be controlled within a ± 5% variation of a standard value.

Friability:

Friability of the tablets was determined using a Roche friabilator. This device subjects the tablets to the combined effect of abrasions and shock in a plastic chamber revolving at 25 rpm, dropping the tablets from a height of 6 inches on each revolution. A preweighed sample of tablets was placed in the friabilator and subjected to 100 revolutions. Tablets were de-dusted using a soft muslin cloth and reweighed.

The friability (F %) is given by the formula

$$\mathbf{F\% = W_0 / W \times 100}$$

Where,

F% = Friability in percentage

W_0 = Initial weight of the tablets before the test

W = weight of the tablets after the test

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Weight variation:
20 tablets remain randomly designated, the average weight stood ascertained, and then they remain weighed individually to calculate the standard deviation.

Drug content:
20 tablets remain balanced and crumpled. An extent of powder corresponding to the quantity of single tablet (50 mg) stood accurately weighed and reassigned to 100ml volumetric flask. Volume was prepared up to the streak through methanol in a 100ml volumetric flask then Solicited intended for 10–15 min. The drug content remain indomitable by UV spectroscopy at a wavelength of 425 nm for Curcumin; 272nm for Bicalutamide [20].

***In vitro* disintegration test for immediate release Curcumin tablets**
Arbitrarily 6 tablets stood designated from the respective lot for disintegration test. Disintegration test remain accomplished deprived of the disc in simulated gastric fluid (37 + 0.50c) expending disintegration apparatus.

- ***In vitro* dissolution studies [22]**

Immediate release Curcumin tablets
It stood conceded out on type II apparatus exhausting the paddle. 500 ml of pH 1.2 buffer (0.1N HCl) as dissolution medium at 37 ± 0.5 °C through the rotational speediness of 50 rpm. The illustrations remain introvert at a determined time interim up to 40 min and analyzed on UV spectrophotometer at 425 nm.

Controlled-release tablets of Bicalutamide
It remains conceded out on type II apparatus expending the paddle. 900 ml of pH 1.2 buffer (0.1N HCl) as dissolution medium at 37 ± 0.5 °C through a rotational speediness of 50 rpm. The sample stood introvert at scheduled period interval adequate 24 h and explored on UV spectrophotometer at 272 nm.

Bi-layer tablet of Curcumin and Bicalutamide
Dissolution of the bilayer tablets remain conceded out on type II apparatus using a paddle. 900 ml of pH 1.2 buffer (0.1N HCl) as dissolution medium at 37 ± 0.50C with a rotational speediness of 50 rpm. The sample stood introvert at scheduled period interval up to 12h and evaluated on UV spectrophotometer by simultaneous estimation method [23].

Statistical analysis of responses
The Surface response plot, Contour plots were drawn using Design Expert Software v 8.0.6.1 (STATEASE).

Stability studies
Stability application of the enhanced preparation remains conceded out as conferring to the ICH recommendations, at 40 ± 2 °C/75 ± 5% RH by adopting Thermo lab TH 90S stability chamber for 3 months. The carried remain observed for drug content, floating behaviour and in vitro drug release profile [25].

RESULT AND DISCUSSION

- **Compatibility studies of drug and polymers**

Fourier transform infrared spectrometry (FTIR)
It was found that there was no possible interaction in between Curcumin and super disintegrant in their original form and mixture form as displayed in Figure 1.
It was found that there was no possible interaction in between Bicalutamide and disintegrant in their original form and mixture form as displayed in Figure 2.

Differential Scanning Calorimetry (DSC)
Compatibility examinations stood similarly conceded by using DSC, which is a qualitative analytical tool for assessing the interactions. The thermo grams indicated no significant change in Curcumin endotherm peaks in mixture samples, as shown in Figure 3.
Compatibility examinations stood similarly conceded by using DSC, which is a qualitative analytical tool for assessing the interactions. The thermo grams indicated no significant change in Bicalutamide endotherm peaks in mixture samples, as shown in Figure 4.

- **Preparation and optimization of bilayer tablets**

The contemporary concerns was carried out to advance a bilayer drug release practice of CCM and BCT to augment absorption and bioavailability through amassed the gastric retention period of the drug. In apprehension towards this method, the crucial requisite remains to undissolved the tablet in a gastric environs and further proceedings for the development of bilayer tablets.
Preformulation study remain toted out expending different concentration level of sodium starch glycolate as a super disintegrant for the immediate release layer and the hydrophilic matrix HPMC-K100.
Optimized formulation N-2from the immediate-release layer and NA-4 from the floating layer was used for the formulation of the bilayer tablet. Direct compression method employed for all formulations was

found to be satisfactory for instance the physicochemical evaluation constraints remained inside the permissible limits.

- **Characterization parameters**

Characterization parameters for immediate release tablets of Curcumin

The thickness of the prepared tablet is in the range of 3.675 ± 0.94 to 2.653 ± 0.45 mm. The hardness of the formulated tablets remain institute in the array of 3.1–3.9 kg/cm2. The friability of all the tablets remain institute to be less than 1%, i.e. in the array of 0.231%–0.426% as displayed in Table 3. The formulation N-3 shows lowest disintegration time 12.51 sec because of its swelling tendency on wetting.

Characterization parameters for floating tablets of BCT

The thickness of the prepared tablet remains in the range of 3.214 ± 0.63 to 3.845 ± 0.62 mm. The hardness of the formulated GRDDS of bicalutamide remains institute in the array of 5.1–5.8 kg/cm2. The friability of entire tablets remain institute to be less than 1%, i.e. in the array of 0.205%–0.419% as displayed in Table 4.

In vitro dissolution studies

The dissolution contour of the preparations containing both the disintegrant was compared. Therefore, formulation N-2 having Xanthan gum in the concentration of 25% remain designated as per the optimized formulation by way of it disintegrates very swiftly in 12.51 s and releases more than 99% drug in 45 min as exhibited in Table 4 and Figure 5. Thus batch N-2 of an immediate-release layer**.**

Formulae NA-4 containing the highest gas-forming agent concentrations and lowest HPMC K4M concentration showed the highest drug release, as shown in Table 5 and Figure 6. These release revisions exposed that the imperative of release remained institute to exist NA-2>NA-5>NA-1>NA-3>NA-4.

For bilayer tablets

Composition of bilayer floating tablet includes an immediate-release layer (N-2 Batch) and controlled release floating layer (NA-4 Batch). The average weight, thickness and hardness of primed tablet remain institute to exist 400 mg, 4.82 mm and 5.1 kg/cm2 correspondingly. The In vitro drug release of the primed bilayer tablets remains institute to stay 99.12% (Curcumin for 45 Min) and 100.16% (Bicalutamide in 24 Hrs.).

Stability studies

Stability study was performed for optimized bilayer tablet formulation at 40 ± 10C and RH 75% for 3 months. The illustrations remain examined for hardness, percent drug content and in-vitro drug release revisions. The results are given in Table 12. And Figure no. 7 substantial variance was perceived for the beyond parameters.

Table 1: Formula for the preparation of Curcumin Granules

Sr. No.	Ingredients	N-1 (mg)	N-2 (mg)	N-3 (mg)
1	Curcumin	100	**100**	100
2	Xanthan gum	55	**50**	45
3	Sodium starch glycolate	16	**16**	16
4	Dicalcium phosphate	24	**24**	24
5	Microcrystalline cellulose	55	**60**	65
	Total weight	250	**250**	250

Table 2: Formula for the preparation of Sustained Release Bicalutamide solid dispersions Tablets

Sr. No.	Ingredients	NA-1 (mg)	NA-2 (mg)	NA-3 (mg)	NA-4 (mg)	NA-5 (mg)
1	Bicalutamide	50	50	50	**50**	50
2	Lactose monohydrate	60.30	70.30	65.30	**65.30**	65.30
3	Sodium starch glycolate	20.80	10.80	20.80	**15.80**	10.80
4	Polyvinyl pyrolidone	2.40	2.40	2.40	**2.40**	2.40
5	Purified water	q.s.	q.s.	q.s.	**q.s.**	q.s.
6	Magnesium stearate	1.5	1.5	1.5	**1.5**	1.5
7	Crospovidone	15	15	10	**15**	20
	Total Weight	**150**	**150**	**150**	**150**	**150**

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Table 3: Evaluation of Immediate Release Cucumin Tablets

Formulation	Thickness± S.D. (mm) (n = 10)	Hardness ± S.D.(kg/cm2) (n = 5)	Friability (%) (n = 10)	Avg. weight variation (n = 20)	Drug content (%)	Disintegration time (in sec) (n = 6)
N-1	3.675 ± 0.94	3.1± 0.5	0.602± 0.4	249.76 ± 1.52	98.33	10.43± 0.95
N-2	2.321 ± 0.32	3.8± 0.6	0.452± 0.1	252.87 ± 0.87	97.09	11.32± 1.12
N-3	**2.653 ± 0.45**	**3.2± 0.9**	**0.542± 0.3**	**251.96 ± 1.76**	**99.59**	**12.51± 1.54**

Table 4: Evaluation of Sustained Release bicalutamide Tablets

Formulation	Thickness± S.D. (mm) (n = 10)	Hardness ± S.D.(kg/cm2) (n = 5)	Friability (%) (n = 10)	Avg. weight variation (n = 20)	Drug content (%)
NA-1	3.214 ± 0.63	5.1± 0.2	0.281± 0.3	149.76 ± 1.42	97.93
NA-2	3.765 ± 0.36	5.8± 0.5	0.214± 0.4	152.87 ± 1.41	99.31
NA-3	3.845 ± 0.62	5.2± 0.1	0.251± 0.2	151.96 ± 0.72	98.32
NA-4	**3.424 ± 0.48**	**5.3± 0.6**	**0.192± 0.2**	**151.96 ± 0.41**	**100.2**
NA-5	3.631 ± 0.93	5.4± 0.2	0.201± 0.8	152.87 ± 0.21	99.31

Table 5: *In vitro* drug release study for Curcumin immediate-release tablets

Time (Minutes)	N-1	N-2	N-3
3	38.54	**42.54**	57.61
5	44.54	**46.32**	61.26
10	48.23	**52.56**	65.62
15	55.89	**59.87**	72.36
20	64.17	**73.21**	82.85
25	69.98	**79.34**	87.41
30	76.42	**84.21**	93.53
35	83.65	**87.76**	97.27
40	88.45	**93.56**	100.54
45	94.56	**98.87**	100.21

Table 6: *In vitro* drug release study for Bicalutamide Sustained-release tablets

Time (Minutes)	NA-1	NA-2	NA-3	NA-4	NA-5
0.5	12.15	10.41	16.90	**18.55**	12.09
1	18.753	13.89	25.89	**26.99**	17.96
2	27.91	17.83	34.69	**35.42**	24.00
4	35.784	21.73	42.38	**43.11**	29.68
8	50.984	32.94	62.70	**61.61**	49.46
10	62.887	45.94	72.78	**73.51**	63.19
12	70.392	52.35	78.09	**78.09**	68.69
16	75.341	59.86	82.67	**86.33**	73.45
20	83.215	64.44	87.61	**92.00**	77.84
24	88.159	68.83	92.00	**97.32**	81.87

Table 7: Stability Data for optimized bilayer tablet formulation

Time (Month)	Evaluation parameters				
	Hardness (kg/cm2)	Drug content (%)		In-vitro drug release	
		Curcumin	Bicalutamide	Curcumin	Bicalutamide
0	5.1	99.56	99.81	99.12	100.16
1	5.0	99.54	99.71	100.01	99.56
2	5.0	99.31	99.67	99.76	99.81
3	4.9	98.81	99.01	99.23	100.02

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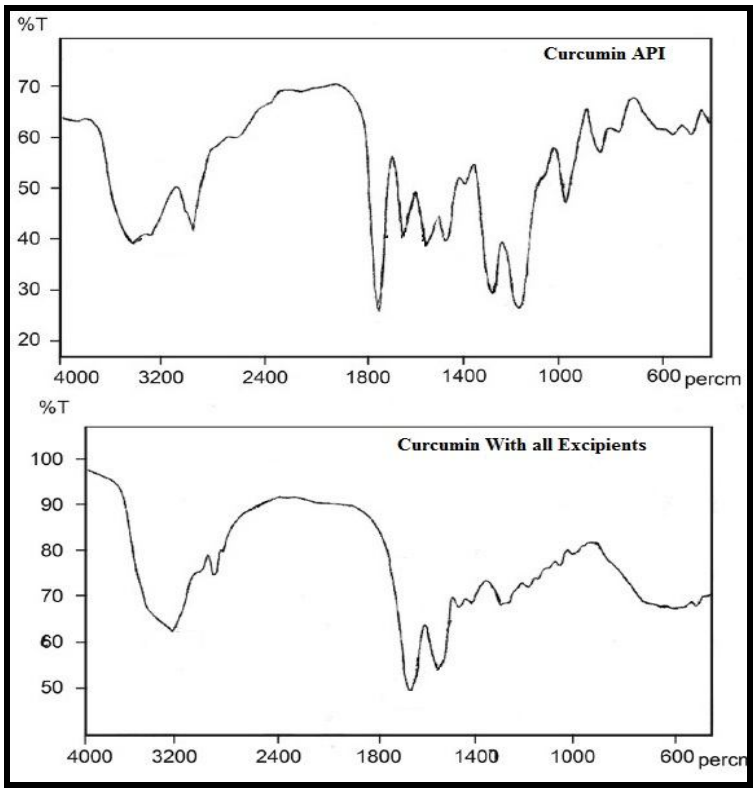

Figure 1: FTIR spectra of Curcumin and Curcumin along with all excipients

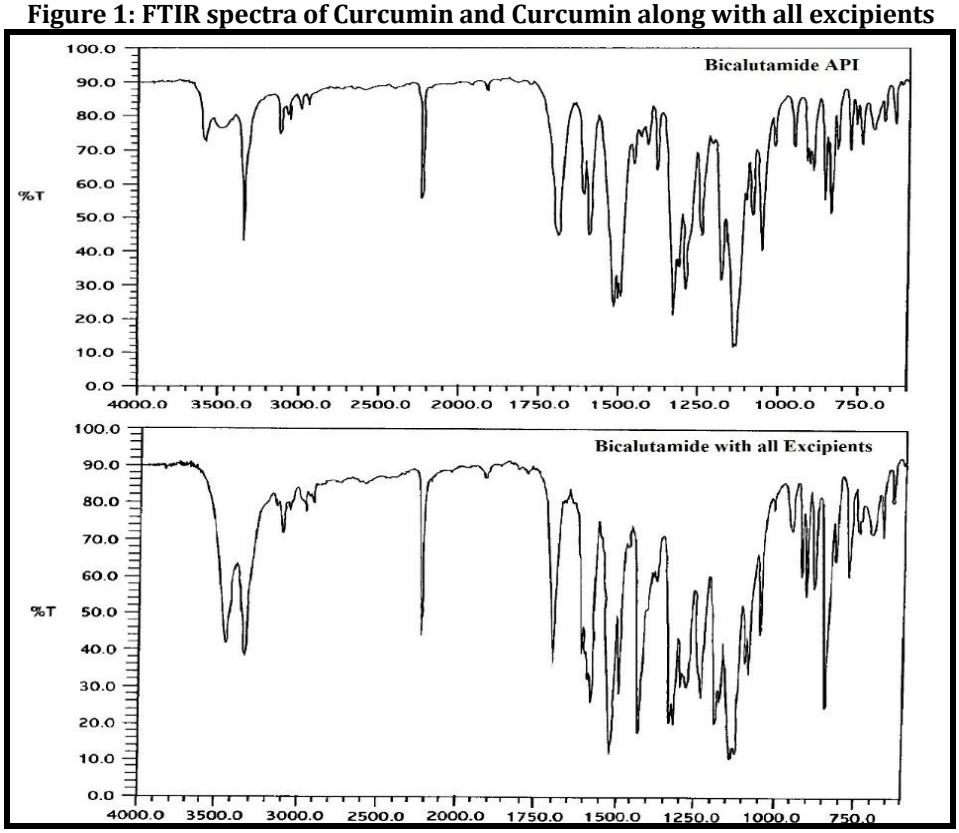

Figure 2: FTIR spectra of Bicalutamide and Bicalutamide along with all excipients

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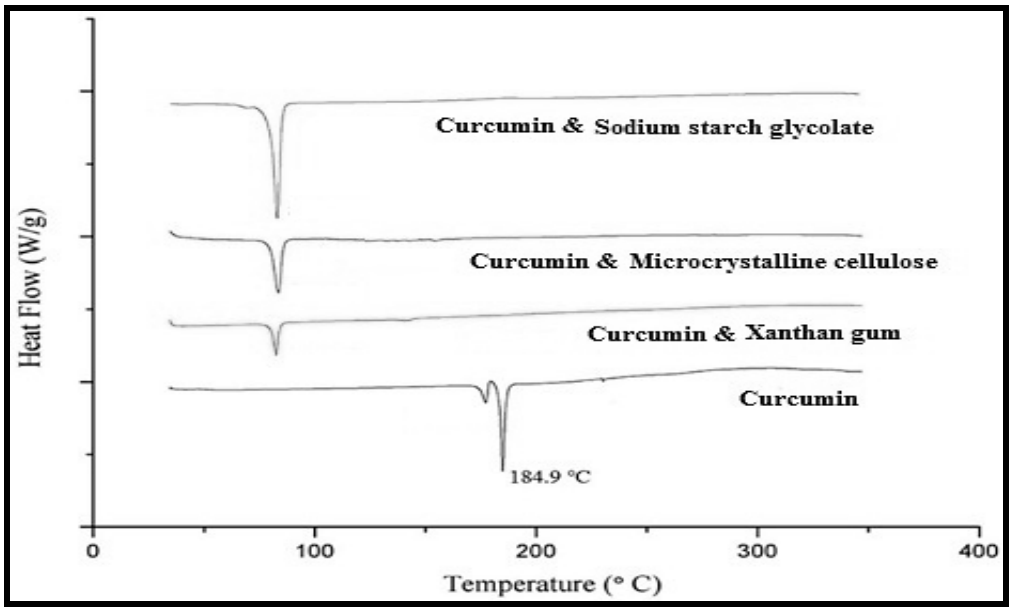

Figure 3: DSC thermo gram of Curcumin and Curcumin along with excipients

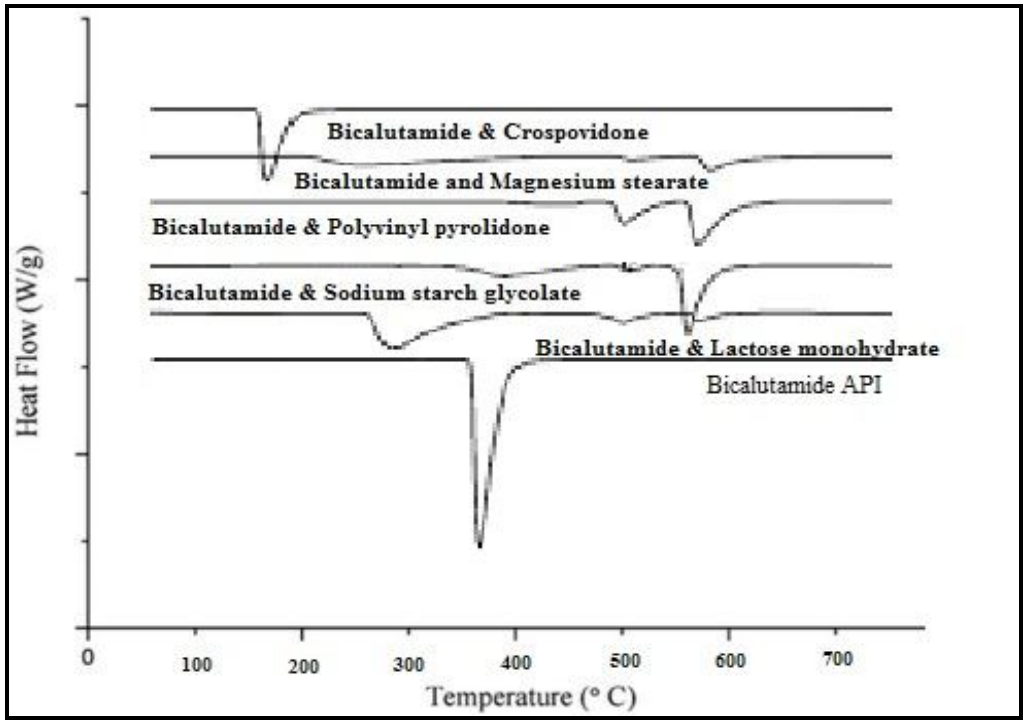

Figure 2: DSC thermo gram of Curcumin and Curcumin along with excipients

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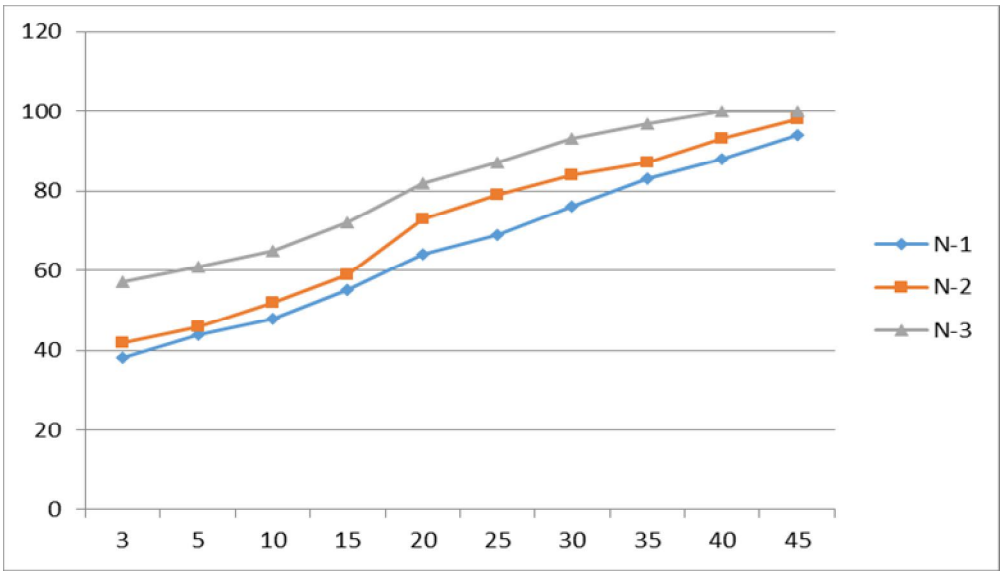

Figure 3: *In vitro* drug release study for Curcumin tablets

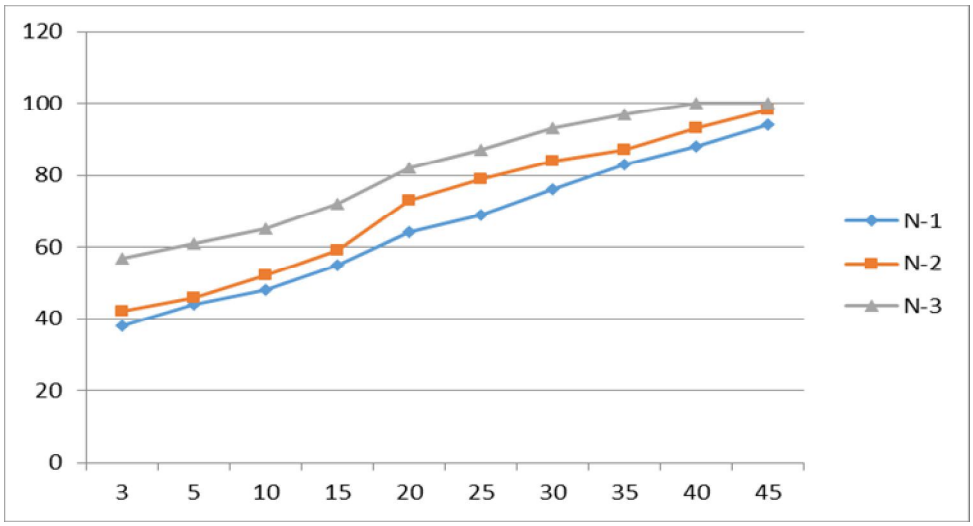

Figure 6: *In vitro* drug release study for Curcumin tablets

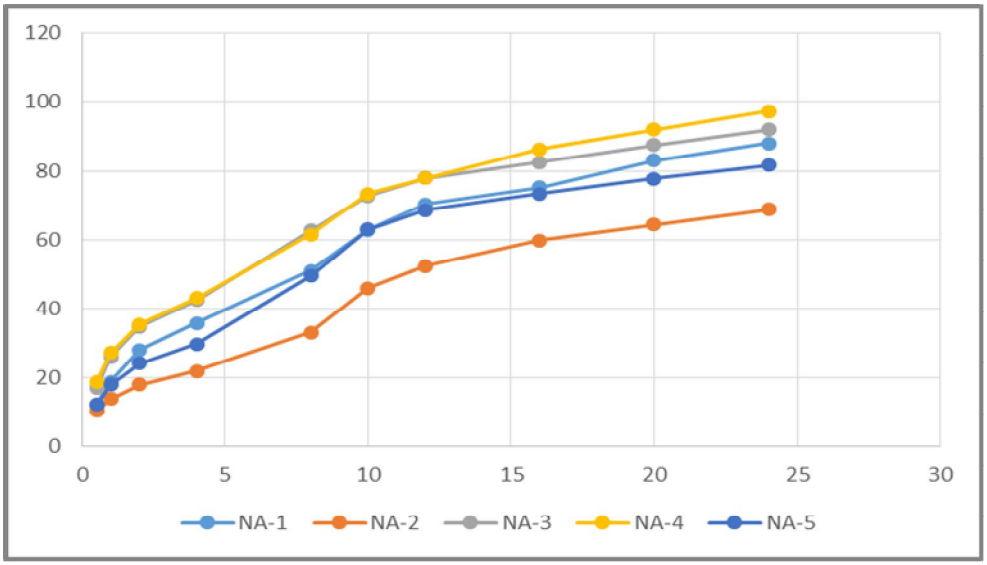

Figure 7: *In vitro* drug release study for Bicalutamide tablets

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DISCUSSION

An effort remained thru to upsurge the oral bioavailability of Curcumin and Bicalutamide fixed-dose combination through retentive the dosage form in the stomach intended for a more extended epoch. This remains accomplished by evolving a gastro retentive sustained release drug delivery system. The precise tablets remain primed to surge the bioavailability of the medications by employing the medications to a complete degree evading avoidable incidence of dosing and consequently the first-pass metabolism. Curcumin and Bicalutamide combination indicated for prostate cancer. Curcumin has been confirmed to exhibit very poor bioavailability, with many studies showing very low, or even undetectable, concentrations in blood and extra intestinal tissue. Bicalutamide is metabolized in the liver and has a very long half-life of 7–10 days.

To achieve patient compliance by controlling blood pressure for an extended duration of time, a bilayer tablet of this fixed-dose combination was suggested. For the formulation of bilayer tablets as well as immediate release layers were optimized separately. Sodium starch glycolate were used as super disintegrant. Microcrystalline cellulose stood practiced as matrix creating gelling agent. Crospovidone adopted as a buoyancy enhancer and release retardant. Other excipients used were Lactose monohydrate, Sodium starch glycolate, Polyvinyl pyrolidone and Magnesium stearate FTIR and DSC thermo grams inveterate the nonappearance of any drug/polymers/excipients interfaces. A physical mixture of medication and polymer were considered by FTIR spectral exploration designed for every physical along with chemical disparity of the medication. From the outcomes, it remain determined that there existed no interfering in the functional groups as the principal peaks of the Curcumin and Bicalutamide remain institute to be intact, designating they stood compatible chemically. Compatibility studies were also carried by using DSC, which is a qualitative analytical tool for assessing the interactions. The thermo grams indicated no substantial amendment in drug endotherm peaks in mixture samples. However, the change in shape and alterations in drugs mixture peak was related to the absorbed moisture by the samples.

Direct compression practice remains engaged to articulate the tablets, since of its cost-clout and owing to reducing the sum of developed strides. The prepared sustained release tablet, immediate-release tablet and bilayer tablets remain assessed for hardness, weight variation, thickness, drug content uniformity, in vitro disintegration time, in-vitro dissolution studies. The floating, immediate and bilayer tablets were compressed using 9.5mm, 4mm, 9.5mm circular flat-faced punches using RIMEK I multi-station rotary punching machine. Floating property revision exposes that all formulations had suitable floating property. All the formulation for more than 24 h because the gel layers, designed through the probed polymers, facilitated proficient entrapment of the engendered gas bubbles. Upsurge in concentration of HPMC-K100 results in the rise of floating lag time because at high-level HPMC-K100 exert probably prevent the access of ways towards the tablet matrix then extend the lag period. Based on various evaluation parameters formulation, N-2 and NA-4 were selected as a composition for bilayer tablet and was further subjected to in vitro release revision, and stability study. The optimized bilayer tablet indicated good stability and values remain inside permitted limits.

CONCLUSION

We have developed a bilayer tablet with an optimized immediate release layer of Curcumin and a sustained release layer of bicalutamide. The tablet shows satisfactory preand post-compression parameters. The strategy of two diverse release phases keep is certainly familiar in together delivery degree and the proportion of the dosage fractions, bestowing to the pharmacokinetics and therapeutic prerequisites. In the immediate-release layer, sodium starch glycolate has a potent effect on in vitro disintegration and in vitro drug discharge. Our data shows that bilayer tablets of Curcumin and bicalutamide might be a suitable treatment for migraine because they allow sequential release of the two drugs. From the result, it was determined that through assuming a systematic preparation advent, conveyance of two drugs out of a distinct dosage practice could be acquired that might expand bioavailability, patient compliance then provide restored disease supervision.

DECLARATION OF COMPETING INTEREST

The authors declare no conflict of interest pertaining to this manuscript.

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REFERENCES

1. Van Rij S, Everaerts W, Murphy DG. (2016) International Trends in Prostate Cancer. In Prostate Cancer (pp. 127-132). Academic Press.
2. Kaler J, Hussain A, Haque A, Naveed H, Patel S. (2020) A Comprehensive Review of Pharmaceutical and Surgical Interventions of Prostate Cancer. Cureus.
3. Mattiuzzi C, Lippi G. (2019) Current cancer epidemiology. Journal of epidemiology and global health. 9(4):217.
4. Rawla P. (2019) Epidemiology of prostate cancer. World journal of oncology; 10(2):63.
5. Yang Q, Fung KM, Day WV, Kropp BP, Lin HK. (2005) Androgen receptor signaling is required for androgen-sensitive human prostate cancer cell proliferation and survival. Cancer cell international 5(1):1-0.
6. Jenster G. (1999) The role of the androgen receptor in the development and progression of prostate cancer. In Seminars in oncology, 26 (4): 407-421.
7. Duvoix A, Blasius R, Delhalle S, Schnekenburger M, Morceau F, Henry E, Dicato M, Diederich M (2005) Chemopreventive and therapeutic effects of Curcumin. Cancer Let 223:181–190.
8. Goel A, Kunnumakkara AB, and Aggarwal BB (2008) Curcumin as "Curecumin": from kitchen to clinic. Biochem Pharmacol 75:787–809.
9. Hatcher H, Planalp R, Cho J, Torti FM, Torti SV (2008) Curcumin: from ancient medicine to current clinical trials. Cell Mol Life Sci 65:1631–1652
10. Goa KL, Spencer CM. (1998) Bicalutamide in advanced prostate cancer: a review. Drugs Aging; 12: 401–22.
11. Blackledge GRP, Cockshott ID, Furr BJA. (1997) Casodex™ (bicalutamide): overview of a new antiandrogen developed for the treatment of prostate cancer. Eur Urol; 31 Suppl. 2: 30–9.
12. Denis L, Mahler C. (1996) Pharmacodynamics and pharmacokinetics of bicalutamide: defining an active dosing regimen. Urology; 47 (1A Suppl.): 26–8.
13. Furr BJ, Tucker H. (1996) The preclinical development of bicalutamide: pharmacodynamics and mechanism of action. Urology; 47 (1A Suppl.): 13–25.
14. Vishal M, Anuj K, Pankaj P, Deepti P, Shraddha S, Mansee S, Dutta M. (2012) Formulation development and evaluation of Bilayer tablets of Lornoxicam. Int. J. Drug Dev. & Res. 4(2):173-9.
15. Panda N, Reddy AV, Reddy GS, Sultana AF. (2015) Formulation design and in vitro evaluation of bilayer sustained release matrix tablets of doxofylline. Int J Pharm Sci.; 7(10):74-83.
16. Abu-Huwaij R, Obaidat RM, Sweidan K, Al-Hiari Y. (2011) Formulation and in vitro evaluation of xanthan gum or carbopol 934-based mucoadhesive patches, loaded with nicotine. Aaps Pharmscitech. 12(1):21-7.
17. Freudenreich O, Goff DC. (2002) Antipsychotic combination therapy in schizophrenia. A review of efficacy and risks of current combinations. Acta Psychiatrica Scandinavica; 106(5):323-30.
18. Smolen JS, Aletaha D, Keystone E. (2005) Superior efficacy of combination therapy for rheumatoid arthritis: fact or fiction. Arthritis and rheumatism; 52(10):2975-83.
19. Felson DT, Anderson JJ, Meenan RF. (1994) The efficacy and toxicity of combination therapy in rheumatoid arthritis. A meta-analysis. Arthritis & Rheumatism: Official Journal of the American College of Rheumatology 37(10):1487-91.
20. Momin S, Khan S, Ghadage DM, Yadav AV, Wagh A. (2017) Formulation and evaluation of bilayer tablets of propranolol hydrochloride. Journal of Drug Delivery and Therapeutics; 7(2):50-7.
21. Singh B, Saini G, Vyas M, Verma S, Thakur S. (2019) Optimized chronomodulated dual release bilayer tablets of fexofenadine and montelukast: quality by design, development, and in vitro evaluation. Future Journal of Pharmaceutical Sciences; 5(1):1-20.
22. Patra C, Kumar A, Pandit H, Singh S, Devi M. (2007) Design and evaluation of sustained release bilayer tablets of propranolol hydrochloride. Acta Pharmaceutica. 57(4):479.
23. Maddiboyina B, Jhawat V, Sivaraman G, Sunnapu O, Nakkala RK, Naik MH, Gulia M. (2020) Formulation Development and Characterization of Controlled Release Core-in-cup Matrix Tablets of Venlafaxine HCl. Current Drug Therapy;15(5):503-11.
24. Kotla NG, Singh S, Maddiboyina B, Sunnapu O, Webster TJ. (2016) A novel dissolution media for testing drug release from a nanostructured polysaccharide-based colon specific drug delivery system: an approach to alternative colon media. International journal of Nano medicine; 11:1089.

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