International Journal of Pharmaceutics and Drug Research
ISSN: 2347-6346
Available online at http://ijpdr.com

Original Research Article

FORMULATIONS AND CHARACTERIZATION OF BILAYER TABLETS OF CILNIDIPINE AND TELMISARTAN USING NATURAL POLYMERS

Ravi Kumar Yadav*, Sheetal Patel
Millanium College of Pharmacy, Bhopal (M.P.)

***Correspondence Info:**
Ravi Kumar Yadav
Millanium College of Pharmacy, Bhopal (M.P.)
Email:
kumarraviyadav707@gmail.com

***Article History:**

Received: 19/04/2026
Revised: 08/05/2026
Accepted: 25/05/2026

ABSTRACT

The present study was designed to formulate and evaluate bilayer tablets of Cilnidipine and Telmisartan using natural polymers to achieve a combination of immediate and sustained drug release for effective management of hypertension. Telmisartan was formulated as an immediate-release layer using superdisintegrants such as sodium starch glycolate, croscarmellose sodium, and crospovidone, while Cilnidipine was incorporated into a controlled-release matrix using natural polymers including guar gum and xanthan gum. Pre-compression studies confirmed acceptable flow and compressibility of all powder blends. Post-compression evaluation showed that all formulations complied with pharmacopeial limits for hardness, friability, weight variation, drug content, and thickness. The optimized formulation demonstrated rapid disintegration and immediate drug release of Telmisartan, whereas Cilnidipine exhibited sustained release up to 12 hours. The *in vitro* release profile confirmed a biphasic drug release pattern, with prompt onset of action from Telmisartan and prolonged antihypertensive effect from Cilnidipine. The study concluded that bilayer tablet technology using natural polymers is an effective approach to improve therapeutic efficacy, reduce dosing frequency, and enhance patient compliance in hypertension management.

Keywords: Bilayer tablets, Cilnidipine, Telmisartan, Natural polymers, Controlled release, Immediate release, Hypertension, Superdisintegrants, Sustained drug delivery, Tablet formulation.

INTRODUCTION

Hypertension is a major chronic cardiovascular disorder and a leading risk factor for heart failure, stroke, and renal complications worldwide. Effective long-term management of blood pressure often requires combination therapy to achieve optimal therapeutic outcomes and reduce cardiovascular risk (Kjeldsen, 2018). Among the widely used antihypertensive agents, Cilnidipine, a calcium channel blocker, and Telmisartan, an angiotensin II receptor blocker (ARB), are frequently prescribed together due to their complementary mechanisms of action. Cilnidipine reduces peripheral vascular resistance by inhibiting L-type calcium channels, while Telmisartan blocks angiotensin II type-1 receptors, thereby suppressing vasoconstriction and aldosterone secretion (Hiremath *et al.*, 2026).

However, conventional immediate-release formulations of these drugs often require multiple daily dosing, which may lead to fluctuations in plasma drug concentration, reduced patient compliance, and suboptimal therapeutic control. To overcome these

limitations, bilayer tablet drug delivery systems have emerged as an effective approach for the delivery of combination drugs with different release profiles (Rahul *et al.,* 2014).

Bilayer tablets consist of two distinct layers, allowing the incorporation of two incompatible or complementary drugs in a single dosage form with controlled and immediate-release characteristics. This system improves dosing convenience, enhances patient adherence, and enables tailored drug release patterns to maintain sustained therapeutic levels (Nikita *et al.,* 2022).

In recent years, there has been growing interest in the use of natural polymers such as xanthan gum, guar gum, pectin, and sodium alginate in tablet formulations due to their biocompatibility, biodegradability, non-toxicity, and cost-effectiveness. These polymers serve as excellent matrix formers and release retardants, enabling controlled drug release while minimizing side effects associated with synthetic polymers (Garala *et al.,* 2025).

The development of a bilayer tablet containing Cilnidipine and Telmisartan using natural polymers is therefore expected to provide a synergistic antihypertensive effect with improved pharmacokinetic and pharmacodynamic profiles. Such a formulation may reduce dosing frequency, enhance patient compliance, and maintain sustained blood pressure control over an extended period (Payghan and Disuza, 2011).

The present study aims to formulate and characterize bilayer tablets of Cilnidipine and Telmisartan using selected natural polymers. The prepared formulations will be evaluated for various physicochemical parameters including hardness, thickness, weight variation, friability, drug content, in vitro dissolution studies, and compatibility studies to ensure their suitability as an effective controlled-release antihypertensive delivery system.

MATERIALS AND METHODS

Material

Cilnidipine and Telmisartan were used as model antihypertensive drugs for the development of bilayer tablets. Sodium starch glycolate, croscarmellose sodium, and crospovidone were employed as superdisintegrants for the immediate release layer, while natural polymers such as guar gum and xanthan gum were used to achieve controlled release in the matrix layer. Microcrystalline cellulose, lactose, PVP K30, talc, and magnesium stearate were used as diluents, binders, glidants, and lubricants to facilitate proper tablet formulation and compression. All chemicals and excipients used were of analytical or pharmaceutical grade.

Methods

Preparation of instant layer of Telmisartan (Phase-1)

Fast dissolving (Instant Layer) tablets of Telmisartan were prepared by direct compression method after incorporating different super disintegrants such as, crosscarmellose sodium (Ac-Di-Sol), crospovidone and sodium starch glycolate in different concentrations. The ingredients given below were weighed and mixed in geometric progression in a dry and clean mortar. Then the ingredients were passed through mesh #60.

Magnesium stearate as lubricant and talc as glidant were added in a final step

and mixed, this blend was subjected to analysis of pre-compression parameters which included Angle of repose, Bulk density, Tap density, Carr's index and Hausner's ratio. The Blend was compressed on 8 mm (diameter) fat punches on a 'Rimek mini press 16 station rotary compression machine. Nine different formulations of Telmisartan were prepared and each formulation contained one of the three disintegrant in different concentration (Maggi *et al.,* 1999). Each tablets weighing 350mg, were obtained. Composition of tablets is mentioned in Table 1

Evaluation of precompression parameter

Bulk density: Both loose bulk density (LBD) and tapped bulk density (TBD) were determined. Accurately weighed amount of granules taken in a 50 ml capacity measuring cylinder was tapped for 100 times on a plane hard wooden surface and estimated the LBD and TBD, calculated by using following formulas (Ahmad *et al.,* 2011).

$$\text{LBD (Loose Bulk Density)} = \frac{\text{Mass of Powder}}{\text{Volume of Packing}}$$

$$\text{TBD (Tapped Bulk Density)} = \frac{\text{Mass of Powder}}{\text{Tapped Volume of Packing}}$$

Compressibility index: Percent compressibility of powder mix was determined by Carr's compressibility index, calculated by using following formula:-

$$\text{Carr's Index \%} = \frac{\text{TBD} - \text{LBD}}{\text{TBD}} \times 100$$

Hausners ratio: It is determined by comparing tapped density to the bulk density by using following equation:-

Housner's ratio = Tapped bulk density/loose Bulk density

Hausner's ratio value <1.25 shows better flow properties

Evaluation of post compression parameter

Shape and colour of tablets

Uncoated tablets were examined under a lens for the shape of the tablet and colour was observed by keeping the tablets in light.

Thickness test

Three tablets were picked from each formulation randomly and thickness was measured individually. It is expressed in mm and standard deviation was also calculated. The tablet thickness was measured using dial-caliper (Mitutoyo, Japan) (Kumar *et al.,* 2012).

Weight variation test

Twenty tablets were selected randomly from each formulation and average weight was determined. The tablets were weighed individually and compared with average weight. The U.S Pharmacopoeia allows a little variation in the weight of a tablet.

Hardness test

The hardness of tablet was measured by Pfizer hardness tester and results were expressed in Kg/cm^2.

Friability test

For this, 20 tablets were taken from each formulation and the friability was determined using Roche friabilator. The equipment was run for 4 min at 25 revolutions per minute. The tablets were taken out, dedusted and reweighted and % friability was calculated. The friability was determined as the mass loss in percent according to Equation:-

$$\%\text{Friability} = (\text{Loss in weight}/\text{Initial weight}) \times 100$$

Uniformity of drug content:

The test is mandatory for tablets with 10mg or less weight of active ingredient. Ten randomly selected tablets from each formulation (F1 to

F9) were finely powdered and Drug equivalent to 10 mg of drug dissolved in 10 ml 0.1 N HCl (Simulated gastric fluid of pH 1.2 without enzymes) sonicate it for 20 minutes, till the entire drug leached out from complex, then the solution was filtered through whatman filter paper No. 41. From this Solution take 1 ml and Diluted up to 100 ml with 0.1 N HCl and the drug content was determined spectrophotometrically at 290nm for Telmisartan.

Method for preparation of Clinidipine controlled release tablets

Direct compression was followed to manufacture the floating tablets of Clinidipine. Eight different formulations (F1, F2, F3, F4, F5, and F6) were prepared by direct compression.

All the polymers selected, drug and excipients were passed through sieve no. 40 before using into formulation. The amount and ratio of drug and polymers were weighed as per given in table No.2 and all the formulation were used for further evaluations parameters (Jayprakash *et al.*, 2011).

Evaluation of tablets

All the tablets were evaluated for following different parameters which includes;

General Appearance

Five tablets from different batches were randomly selected and organoleptic properties such as color, odor, taste, shape, were evaluated. Appearance was judged visually. Very good (+++), good (++), fair (+) poor (-), very poor (- -) (Karwa and Kasture, 2011).

Thickness and diameter

Thickness and diameter of tablets were determined using Vernier caliper. Five tablets from each batch were used, and an average value was calculated.

Drug content

Twenty tablets were taken and amount of drug present in each tablet was determined. The tablets were crushed in a mortar and the powder equivalent to 100mg of drug was transferred to 100ml standard flask. The powder was dissolved in 50 ml of 0.1 N HCl and made up to volume with of 0.1 N HCl.

The sample was mixed thoroughly and filtered through a 0.45µ membrane filter. The filtered solution was diluted suitably and reacts with dye and analyzed for drug content by UV spectrophotometer at a λ_{max} of 240nm using of 0.1 N HCl as blank.

Hardness

For each formulation, the hardness of five tablets was determined using the Monsanto hardness tester (Cadmach).

Friability

The friability of a sample of 10 tablets was measured using a Friability tester (Electro Lab). Ten tablets were weighed, rotated at 25 rpm for 4 minutes. Tablets were reweighed after removal of fines (dedusted) and the percentage of weight loss was calculated.

Uniformity of weight

Twenty tablets were randomly selected from each batch individually weighed, the average weight and standard deviation of 20 tablets was calculated (Yin *et al.*, 2014).

Dissolution rate studies

In vitro drug release of the sample was carried out using USP- type II dissolution apparatus (Paddle type). The dissolution medium, 900 ml 0.1N HCl was placed into the dissolution flask maintaining the temperature of 37±0.50ºC and rpm of 75. One Clinidipine tablet was placed in each basket of dissolution

apparatus. The apparatus was allowed to run for 12 hours. Sample measuring 5 ml were withdrawn after every 1 hour up to 12 hours using 10ml pipette. The fresh dissolution medium (37ºC) was replaced every time with the same quantity of the sample. From this take 0.5 ml and dilute up to 10 ml with 0.1 N HCl and take the absorbance at 240nm using spectroscopy.

Formulation development of bilayer tablet

Optimized formulation IF-7 of Instant release layer and optimized formulation of F-5 for control release used for formulation of Bi-layer tablet.

Evaluation of bilayer tablets

All the tablets were evaluated for following different parameters which includes;

General appearance

Five tablets from different batches were randomly selected and organoleptic properties suchas color, odor, taste, shape, were evaluated. Appearance was judged visually (Ohmori and Makino, 2004).

Very good (+++), good (++), fair (+) poor (-), very poor (- -).

Thickness and diameter

Thickness and diameter of tablets were determined using Vernier caliper. Five tablets from each batch were used, and an average value was calculated.

Hardness

For each formulation, the hardness of five tablets was determined using the Monsanto hardness tester (Cadmach).

Friability

The friability of a sample of 10 tablets was measured using a Friability tester (Electro Lab). Ten tablets were weighed, rotated at 25 rpm for 4 minutes. Tablets were reweighed after removal of fines (dedusted) and the percentage of weight loss was calculated.

Uniformity of weight

Twenty tablets were randomly selected from each batch individually weighed, the average weight and standard deviation of 20 tablets was calculated (Pandey *et al.*, 2007).

Drug content

Twenty tablets were taken and amount of drug present in each tablet was determined. The tablets were crushed in a mortar and the powder equivalent to 10mg of Clinidipine was transferred to 10ml standard flask. The powder was dissolved in 10 ml of 0.1 N HCl and made up to volume with 0.1 N HCl. The sample was mixed thoroughly and filtered through a 0.45µ membrane filter. The filtered solution was further diluted 0.2 ml to 10 ml suitably 10 ppm solutions of and determines the Conc. of drug at 290nm for Telmisartan and 240nm for Clinidipine.

Dissolution rate studies

In vitro drug release was performed according to the USP dissolution apparatus II at 50 rpm and 37±0.5ºC temperature over a 12 hrs period for Telmisartan and Clinidipine bilayer tablets using an automated paddle dissolution system (Labindia) (Peppas and Korsmeyer, 1987; Korsmeyer *et al.*, 1986). A minimum of 6 tablets per batch were tested. The media used was 0.1N HCl at a pH 1.2 and a volume of 900 ml was maintained at 37±0.5ºC. Test sample (1ml) was withdrawn at particular time interval and replaced with fresh dissolution media maintained at the same temperature and the concentration of dissolved drug was determined using U.V. (Labindia 3000 plus) spectrophotometer.

RESULTS AND DISCUSSION

The present study was undertaken to develop and evaluate bilayer tablets of Cilnidipine and Telmisartan using natural polymers, aimed at achieving immediate release of Telmisartan and controlled release of Cilnidipine for effective antihypertensive therapy. The formulation strategy successfully combined fast disintegrating and sustained-release layers within a single dosage form, thereby improving therapeutic efficiency and patient compliance.

The pre-compression evaluation of Telmisartan formulations (Table 3) showed that all powder blends exhibited acceptable flow properties suitable for direct compression. The loose bulk density ranged from 0.315 to 0.345 g/ml, while tapped density ranged from 0.422 to 0.454 g/ml, indicating uniform packing characteristics. Carr's Index values (24.01–27.96%) and Hausner's ratio (1.316–1.388) suggested fair to passable flowability, which is adequate for tablet manufacturing without significant processing issues.

Similarly, pre-compression properties of Cilnidipine formulations (Table 6) demonstrated good flow behavior, with compressibility index values ranging from 19.784 to 21.805% and Hausner's ratios between 1.247 and 1.279. These values indicate acceptable compressibility and ensure uniform die filling during compression.

Post-compression evaluation of Telmisartan fast dissolving tablets (Table 4) revealed that all formulations complied with pharmacopeial limits. Hardness values ranged from 3.2 to 3.6 kg/cm², ensuring adequate mechanical strength. Friability values were below 1% in all formulations, confirming sufficient resistance to abrasion. Drug content ranged from 96.12% to 99.25%, indicating uniform drug distribution. Tablet thickness remained consistent (2.1–2.4 mm), suggesting good compression uniformity.

For Cilnidipine controlled release tablets (Table 7), hardness values ranged from 5.1 to 5.4 kg/cm², indicating stronger matrix formation suitable for sustained release. Friability values remained below 1%, confirming mechanical integrity. Drug content was within acceptable limits (95.45–99.12%), demonstrating uniform drug dispersion within the polymer matrix.

The disintegration time of Telmisartan formulations (Table 5) ranged from 48 to 88 seconds. Among all formulations, IF7 showed the fastest disintegration (48 ± 2 sec), which may be attributed to the optimal concentration of superdisintegrant (crospovidone). Rapid disintegration is essential for immediate drug release and faster onset of action in hypertensive emergencies.

The in-vitro release profile of Cilnidipine controlled release tablets (Table 8) demonstrated sustained drug release behavior over 12 hours. Formulation F5 showed a controlled and extended release pattern, with 98.12% drug release at 12 hours, indicating successful matrix formation using natural polymers such as guar gum and xanthan gum.

For bilayer tablets (Table 11), Telmisartan exhibited rapid release, achieving 97.78% drug release within 1.5 hours, confirming immediate release behavior. In contrast, Cilnidipine showed a prolonged release profile, reaching 98.85% release at 12 hours. This biphasic release pattern confirms the successful design of the bilayer system, where the immediate release layer provides rapid

therapeutic onset, and the sustained layer maintains prolonged drug levels.

The optimized bilayer formulation (Table 9) exhibited acceptable physical characteristics including hardness (5.8 kg/cm²), friability (0.668%), uniform weight variation, and consistent thickness (5.12 mm). Drug content analysis (Table 10) showed high content uniformity for both Telmisartan (98.85%) and Cilnidipine (99.45%), confirming formulation reliability.

Table 1: Composition of Telmisartan fast dissolving tablets

Ingredients(mg)	Formulation code								
	IF1	**IF 2**	**IF 3**	**IF 4**	**IF 5**	**IF 6**	**IF 7**	**IF 8**	**IF 9**
Telmisartan	10	10	10	10	10	10	10	10	10
Sodium Starch glycolate	10	15	20	-	-	-	-	-	-
Croscarmellose sodium	-	-	-	10	15	20	-	-	-
Crospovidone	-	-	-	-	-	-	10	15	20
Microcrystalline cellulose	65	60	55	65	60	55	65	60	55
Talc	5	5	5	5	5	5	5	5	5
Magnesium stearate	10	10	10	10	10	10	10	10	10
Total weight	100	100	100	100	100	100	100	100	100

Table 2: Various formulations of Clinidipine controlled release tablets

Excipients (mg)	**F1**	**F2**	**F3**	**F4**	**F5**	**F6**
Clinidipine	10	10	10	10	10	10
Guar gum	90	120	-	-	45	60
Xanthan Gum	-	-	90	120	45	60
PVP K30	15	15	15	15	15	15
Talc	5	5	5	5	5	5
Magnesium Stearate	10	10	10	10	10	10
Lactose	70	40	70	40	70	40
Total Weight	200	200	200	200	200	200

Table 3: Results of pre-compressional parameters of Telmisartan

Formulation code	Parameters			
	Loose Bulk density(gm/ml)	Tapped bulk density(gm/ml)	Carr's Index (%)	Hausner's Ratio
IF1	0.315	0.425	25.88	1.349
IF2	0.325	0.431	24.59	1.326
IF3	0.336	0.446	24.66	1.327
IF4	0.345	0.454	24.01	1.316
IF5	0.322	0.447	27.96	1.388
IF6	0.319	0.428	25.47	1.342
IF7	0.324	0.431	24.83	1.330
IF8	0.325	0.429	24.24	1.320
IF9	0.316	0.422	25.12	1.335

Table 4: Results of post-compression parameters of all formulations

F. Code	Hardness test (kg/cm^2)	Friability (%)	Weight variation (%)	Thickness (mm)	Drug content (%)
IF1	3.2±0.3	0.745±0.015	98±6	2.2±0.1	98.85±0.25
IF2	3.3±0.2	0.698±0.032	95±4	2.2±0.4	97.85±0.36
IF3	3.4±0.6	0.715±0.022	96±2	2.3±0.5	96.12±0.25
IF4	3.5±0.5	0.795±0.016	99±3	2.4±0.3	96.65±0.63
IF5	3.2±0.4	0.663±0.036	101±2	2.3±0.2	98.74±0.41
IF6	3.6±0.3	0.712±0.025	99±3	2.3±0.1	96.65±0.36
IF7	3.4±0.2	0.698±0.014	98±6	2.4±0.4	99.25±0.32
IF8	3.6±0.2	0.652±0.032	102±4	2.3±0.6	98.74±0.44
IF9	3.4±0.2	0.663±0.22	98±5	2.1±0.5	98.36±0.25

Table 5: Results of Disintegration time of instant layer of Telmisartan

Formulation code	Disintegration time (sec.) (n=3) Mean ± SD
IF1	88±6
IF2	79±7
IF3	65±6
IF4	80±5
IF5	65±6
IF6	55±3
IF7	48±2
IF8	55±5
IF9	62±4

Table 6: Result of pre-compression properties of Clinidipine tablets

F. Code	Bulk density(gm/ml)	Tapped density(gm/ml)	Compressibility index	Hausner ratio
F1	0.442	0.556	20.504	1.258
F2	0.416	0.532	21.805	1.279
F3	0.435	0.547	20.475	1.257
F4	0.452	0.569	20.562	1.259
F5	0.436	0.549	20.583	1.259
F6	0.446	0.556	19.784	1.247

Table 7: Results of post compression properties of Clinidipine tablets

F. code	Thickness (mm)	Hardness (kg/cm^2)	Weight variation (mg)	Friability (%)	Drug content (%)
F1	3.1±0.2	5.3±0.2	200±6	0.758±0.036	98.45±0.15
F2	3.3±0.3	5.2±0.3	198±8	0.698±0.025	98.74±0.32
F3	3.2±0.4	5.4±0.2	195±5	0.745±0.042	96.65±0.65
F4	3.1±0.2	5.2±0.2	202±3	0.773±0.022	95.45±0.25
F5	3.1±0.4	5.3±0.0.3	199±4	0.785±0.036	99.12±0.41
F6	3.2±0.3	5.1±0.2	201±7	0.732±0.047	98.14±0.32

Table 8: *In-vitro* drug release study of tablets

S. No.	Time (hr)	% Cumulative drug release
		F5
1	0.5	11.25
2	1	20.36
3	1.5	32.25
4	2	40.36
5	3	55.65
6	4	65.58
7	6	73.32
8	8	88.98
9	12	98.12

Table 9: Post-compression parameters of optimized formulation

Formulation	Hardness test (kg/cm^2)	Friability (%)	Weight variation	Thickness (mm)
1.	5.8	0.668	Passes	5.12

Table 10: Results of Drug content analysis

Formulation	Telmisartan (% Label Claim)	Clinidipine (% Label Claim)
In-house Bilayer tablet	98.85	99.45

Table 11: Results of Dissolution rate studies of bilayer tablets

Time (Hour)	% Drug Release	
	Telmisartan	Clinidipine
0.5	45.58	13.36
1	59.98	20.25
1.5	97.78	30.36
2	-	42.25
4	-	55.65
6	-	69.98
8	-	73.32
10	-	81.15
12	-	98.85

CONCLUSION

The present study successfully developed and evaluated bilayer tablets of Cilnidipine and Telmisartan using natural polymers for the management of hypertension. The formulation provided a rapid release of Telmisartan for immediate antihypertensive action, while Cilnidipine showed sustained release for prolonged therapeutic effect. All formulations exhibited satisfactory pre- and post-compression properties with acceptable drug content, mechanical strength, and uniformity. The optimized bilayer tablet demonstrated a biphasic release profile, confirming the effectiveness of the designed system. It can be concluded that bilayer tablet technology using natural polymers is a promising approach to improve drug release characteristics, enhance therapeutic efficacy, and increase patient compliance.

DECLARATION OF INTEREST

The authors declare no conflicts of interests. The authors alone are responsible for the content and writing of this article.

REFERENCES

- Hiremath, J., Kirpalani, A., Chafekar, D., Jayagopal, P. B., Ray, S., Chopra, V. K., Dani, S., Tripathi, K., Sawhney, J. P., Oomman, A., & Sathe, S. (2026). Hypertension management beyond blood pressure control in India: An expert consensus on angiotensin II receptor blocker and calcium channel blocker combination therapy with reference to telmisartan and cilnidipine. *Cureus, 18*(2).

- Kjeldsen, S. E. (2018). Hypertension and cardiovascular risk: General aspects. *Pharmacological Research, 129*, 95–99.
- Rahul, M., Patil, S., Shetkar, M., Chavan, D., & Bhagwat, P. (2014). A review on immediate release drug delivery systems. *PharmaTutor, 2*(8), 95–109.
- Nikita, S., Deepak, J., Vikas, J., & Pradeep, P. (2022). A review on applications of bilayer tablet technology for drug combinations. *Journal of Drug Delivery and Therapeutics, 12*(1), 222–227.
- Garala, K., Ughreja, R., Ranpara, R., & Dholaria, N. (2025). Optimizing bioavailability through natural excipients: A sustainable approach to drug delivery. In *Innovative pharmaceutical excipients: Natural sources* (pp. 321–343).
- Payghan, S. A., & Disuza, J. I. (2011). Formulation, evaluation and development of bilayer tablet. *International Journal of Pharmaceutical Research and Development, 3*, 80–87.
- Maggi, L., Machiste, E. O., Torre, M. L., & Conte, U. (1999). Formulation of biphasic release tablets containing slightly soluble drugs. *European Journal of Pharmaceutics and Biopharmaceutics, 48*, 37–42.
- Ahmad, Q. J., Hariprasana, R. C., & Kulkarni, U. (2011). Design and evaluation twice daily lornoxicam bilayer matrix tablets by using hydrophilic polymer sodium alginate. *Asian Journal of Biochemical and Pharmaceutical Research, 2*, 552–561.
- Kumar, H. G., Jagannathan, K., Sambath, R., & Perumal, P. (2012). Formulation and in vitro evaluation of bilayer floating tablets of metformin hydrochloride and sitagliptin phosphate. *International Journal of Advanced Pharmaceutics, 2*, 64–81.
- Jayprakash, S., Mohamed, H. S., Kulathuran, P. K., Vignesh, N., Mohmd Firthouse, P. U., & Bhoopathi, M. (2011). Formulation and evaluation of bilayer tablet of metformin hydrochloride. *Asian Journal of Pharmaceutical and Health Sciences, 1*, 183–188.
- Karwa, P., & Kasture, P. V. (2011). Formulation and in vitro evaluation of bilayer tablet of zolpidem tartrate for biphasic drug release. *International Journal of PharmTech Research, 3*, 1919–1929.
- Yin, L., He, W., Li, Y., Zhang, R., & Wu, Z. (2014). Gastro-floating tablets for the sustained release of metformin and immediate release of pioglitazone: Preparation and in vitro/in vivo evaluation. *International Journal of Pharmaceutics, 476*, 223–231.
- Ohmori, S., & Makino, T. (2004). Formulation of bilayer tablets of phenylpropanolamine containing HPMC 2208 matrix. *Acta Pharmaceutica, 36*, 49–57.
- Pandey, H., Tiwari, V. K., & Prajapati, S. K. (2007). Sustained release bi-layered tablets of domperidone maleate using the hydrophilic matrix system. *Indian Drugs, 44*(4), 261–263.