Table 7: Evaluation parameter of factorial batches

Batch code	Weight variation (mg)	Hardness (kg/cm²)	Thickness (mm)	% Drug content	Friability (%)	Buoyancy lag time (sec)
F1	192.39 ± 2.38	2.00 ± 0.15	2.10 ± 0.025	100.20 ± 0.59	0.148	129
F2	196.71 ± 2.98	2.75 ± 0.26	1.92 ± 0.032	99.00 ± 1.04	0.020	93
F3	192.6 ± 2.86	2.00 ± 0.12	2.26 ± 0.031	97.00 ± 1.27	0.289	66
F4	197.37 ± 2.07	2.75 ± 0.17	2.05 ± 0.070	98.55 ± 0.93	0.90	58
F5	196.41 ± 3.89	2.00 ± 0.25	2.30 ± 0.045	99.50 ± 0.63	0.57	41
F6	193.21 ± 1.97	1.50 ± 0.15	1.90 ± 0.036	100.10 ± 0.73	0.573	182
F7	198.81 ± 3.02	2.75 ± 0.21	1.80 ± 0.062	100.80 ± 0.67	0.43	94
F8	193.62 ± 2.42	3.00 ± 0.10	1.90 ± 0.035	101.10 ± 0.95	0.91	102

Table 8: *In vitro* drug release profile of factorial batches

Time (h)	Cumulative percentage release (CPR)							
	F1	F2	F3	F4	F5	F6	F7	F8
0	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
0.25	15.89	10.45	14.29.	4.52	20.35	15.49	15.49	3.91
0.5	23.64	14.04	24.09	10.48	37.71	27.94	18.92	10.74
1	35.82	19.16	29.73	14.18	52.44	32.08	26.93	12.69
2	38.35	34..67	45.65	19.14	69.89	44.2	32.24	15.79
3	52.83	48.54	52.28	24.05	78.33	55.67	40.34	17.62
4	58.52	51.05	58.47	28.63	82.45	58.07	48.54	21.47
5	66.82	55..2	68.82	30.54	85.8	68.66	56.86	25.16
6	70.44	58.38	75.27	35.15	90.51	82.18	60.24	27.75
7	79.14	74.67	83.7	35.33	93.25	86.38	72.44	30.73
8	87.36	83.38	87.65	41.32	96.69	93.94	79.19	33.15
9	90.84	86.31	90.36	43.2	100.7	98.76	83.45	35.27
10	92.04	88.74	93.6	48.13	97.64	100.82	89.98	41.81
11	95.01	90.68	96.36	52.43	96.86	98.28	98.75	43.43
12	98.02	91.44	98.11	56.72	96.30	96.47	99.98	46.43

Table 9: Kinetic treatment of dissolution data

	F1	F2	F3	F4	F5	F6	F7	F8
Zero order								
b	7.194	7.469	7.46	3.528	4.922	8.357	7.380	2.915
a	28.487	28.423	28.423	12.529	58.283	27.093	18.678	9.828
R^2	0.9859	0.9721	0.9721	0.9791	0.8693	0.9841	0.9936	0.995
First order								
b	−0.105	−0.109	−0.109	−0.022	−0.146	−0.187	−0.081	0.055
a	1.998	1.995	1.995	1.9499	1.8141	2.226	2.007	1.086
R^2	0.9477	0.9809	0.9809	0.9860	0.9791	0.8435	0.9585	0.970
Higuchi								
b	29.312	30.873	30.87	14.50	21.002	34.201	29.867	11.838
a	1.578	−0.456	−0.455	−0.939	37.843	−4.482	−8.487	−0.991
R^2	0.9784	0.9927	0.9927	0.9888	0.9460	0.9850	0.9726	0.9809
Hixon Crowell								
b	0.243	0.253	0.252	0.069	0.2613	−0.353	0.2098	−0.120
a	0.257	0.263	0.2630	0.185	0.9431	−0.008	20.134	2.375
R^2	0.9771	0.9927	0.9927	0.9846	0.9777	0.9490	0.9781	0.9822
Korsemeyer and Peppas								
a	−0.494	−0.517	−0.517	−0.859	−0.254	−0.508	−0.621	−0.936
n	0.457	0.505	0.506	0.5091	0.269	0.5199	0.545	0.487
R^2	0.9584	0.9931	0.9931	0.9930	0.9696	0.9868	0.9682	0.9703

b = Slope, a = Intercept, R^2 = Correlation coefficient, n = Diffusion exponent

release [Table 9]. For batches F2, F3, F4, F6, and F7, the values of n were 0.505, 0.506, 0.5091, 0.5199, and 0.545, respectively, indicating non-Fickian release; whereas for batches F1, F5, and F8, the values of n were 0.457, 0.269, and 0.487, respectively, indicating Fickian release. F7 batch gave zero-order release.

Dissolution data of all batches were subjected to find f_2 similarity for the selection of optimum batch. Theoretical profile of stavudine was taken as reference. F7 batch showed maximum similarity (70.91) compared with other batches [Table 10]. Hence, formulation F7 was optimized based on the highest f_2 similarity (70.91) it showed zeroorder drug release.

Drug–excipient compatibility study was carried out using FT-IR 1700 (Shimadzu) and DSC-60 (Shimadzu). Drug–excipient interaction plays a vital role in the release of drug

from formulation. The drug exhibits carbonyl peak (C=O) at 1647.10 cm^{-1}, alkyl peak (=C–H) at 3024.18 cm^{-1}, and carbonyl amide group peak (N–H) at 3417.63 cm^{-1}. It was observed that there were no changes in these main peaks in the IR spectra of a mixture of drug and excipient [Figures 1 and 2].

DSC thermograms were obtained for pure stavudine and mix matrix floating tablet containing stavudine and other excipients. Pure powdered stavudine showed a melting endotherm at 172.10°C [Figure 3]. DSC thermograms of floating tablet showed the melting peak of the drug at 169.36°C [Figure 4]. There was no significant difference in the melting point of drug in both samples. It indicates that the drug was present in its characteristic physical and chemical form. It was compatible with all the excipients present in the tablet and there was no major interaction of the drug with the excipients.

Table 10: Comparison of *in vitro* drug release after stability study

Time (h)	CPR (initial) F7	CPR (after storage at 40 ± 2°C/75 ± 5% RH) after 1 month
1	26.93	28.34
2	32.24	34.16
3	40.34	43.68
4	48.54	46.98
5	56.86	57.23
6	60.24	65.41
7	72.44	69.30
8	79.19	75.74
9	83.45	81.39
10	89.98	89.45
11	98.75	96.17
12	99.98	98.44

Stability study was carried out by storing optimized formulation at 40 ± 2°C and 75 ± 5% RH for 1 month. At the end of the studies, samples were analyzed for the drug content, *in vitro* drug release, and floating lag time. There was not any change in morphological condition during the stability study and also not any measurable change in the remaining parameter, as shown in Table 7. *In vitro* drug release was 98.44% after 12 h [Figure 5]. Similarity factor of the batch after stability study was 77.09, which was comparable to the initial drug release profile.

CONCLUSION

It can be concluded from this study that the combined mix matrix system containing hydrophobic and hydrophilic polymer minimized the burst release of drug from the tablet and achieved a drug release by zero-order kinetics, which is practically difficult with only hydrophilic matrix. Bees wax used as hydrophobic material and HPMC K4M as hydrophilic material gave zero-order release of stavudine mix matrix floating tablet.

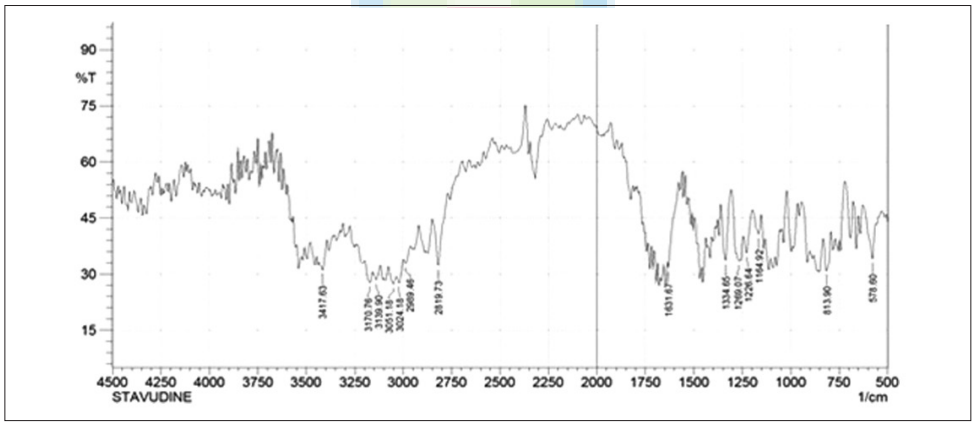

Figure 1: FT-IR spectrum of stavudine

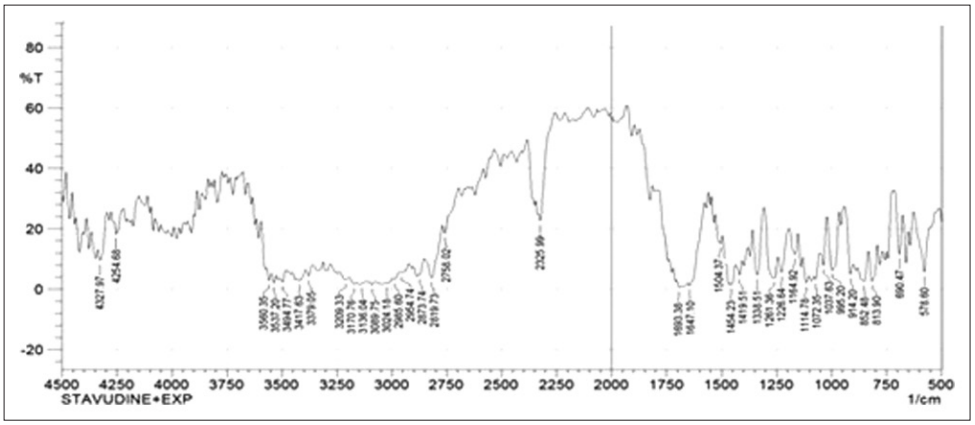

Figure 2: FT-IR spectrum of stavudine & excipients

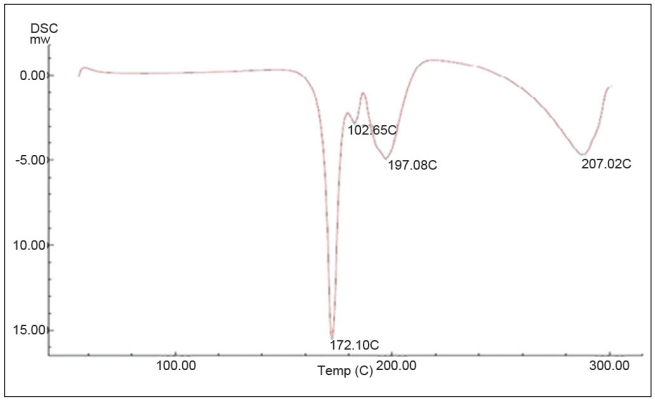

Figure 3: DSC thermogram of stavudine

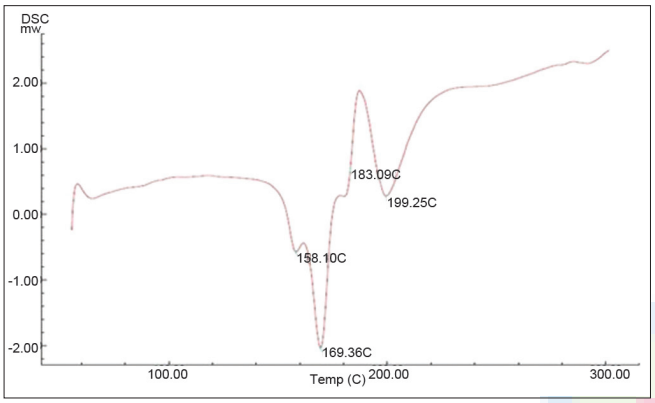

Figure 4: DSC thermogram of stavudine mix matrix floating tablet

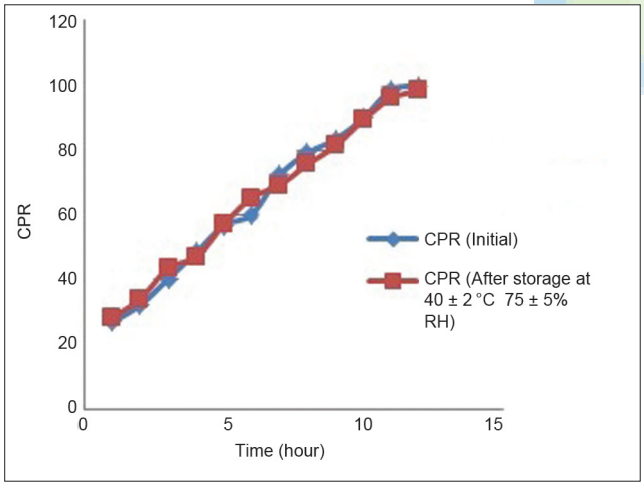

Figure 5: Comparison of release profile initially and after stability studies

Ethyl cellulose and sodium bicarbonate were used as floating enhancers and gave a total floating time of more than 12 h. From the regression analysis, insignificant factors were omitted. Formulation F7 was selected as an optimum formulation as it showed more similarity in dissolution profile with theoretical profile (similarity factor, $f_2 = 70.91$). The dissolution of batch F7 can be described by zero-order kinetics ($R^2 = 0.9936$) with anomalous (non-Fickian) diffusion as a release mechanism ($n = 0.545$). There was no difference observed in the release profile after temperature sensitivity study at 40°C/75% RH for 1 month.

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