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Development and Evaluation of Orodispersible Tablets of Drotaverine HCl Using Sublimation Technique for Enhanced Disintegration and Drug Release

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ABSTRACT

The study aimed to develop and evaluate orodispersible tablets (ODTs) of Drotaverine HCl using sublimation technique to achieve faster disintegration and enhanced drug release. Spectroscopic analysis confirmed a linear correlation between drug concentration and absorbance (r=0.999) in 0.1N HCl and pH 6.8 phosphate buffer. Three superdisintegrants—Avicel PH101, sodium starch glycolate, and croscarmellose sodium—were evaluated, with croscarmellose sodium (4%) showing optimal flow properties (angle of repose: 20.28°, Carr's index: 7.6). Sublimation agents (camphor, menthol, and their combination) were incorporated, and tablets exposed to 40°C for 5 hours exhibited the shortest disintegration time (6.3 sec). Formulation DCM2 (camphor + menthol) demonstrated rapid drug release (100.16% in 5 min) and passed stability tests (30±2°C/70±5% RH and 40±2°C/75±5% RH for 6 months). DSC, XRD, and FTIR studies confirmed drug-excipient compatibility. The study concluded that DCM2 is a stable and effective ODT formulation for rapid drug delivery.

INTRODUCTION

Drotaverine HCl, a potent antispasmodic agent, is used to treat gastrointestinal and urinary tract spasms. Conventional tablets face challenges like slow disintegration and delayed onset of action. Orodispersible tablets (ODTs) offer a solution by dissolving rapidly in the mouth, enhancing patient compliance, especially for pediatric and geriatric populations. This study focused on developing Drotaverine HCl ODTs using sublimation technology to improve disintegration and dissolution. Superdisintegrants (Avicel PH101, sodium starch glycolate, croscarmellose sodium) and sublimating agents (camphor, menthol) were evaluated for their effects on tablet properties. The study also included spectroscopic validation, pre-compression parameter analysis, and stability testing to ensure formulation efficacy and compatibility.

MATERIALS

Drug: Drotaverine HCl

Superdisintegrants: Avicel PH101, sodium starch glycolate, croscarmellose sodium

Sublimating agents: Camphor, menthol

Other excipients: Mannitol, polyvinylpyrrolidone, magnesium stearate, HPMC 3 cps, aspartame.

METHODS

Spectroscopic Analysis:
Calibration curves were plotted in 0.1N HCl and pH 6.8 phosphate buffer (0–40 µg/mL). Absorbance was measured using UV spectroscopy.

Formulation of ODTs:
Granule Preparation: Wet granulation method was employed.

Flow Properties: Angle of repose, Carr's index, and Hausner ratio were evaluated.

Tablet Compression: Tablets were prepared using sublimation technique with varying superdisintegrant concentrations (2–4%).

Optimization of Sublimation:
Tablets were exposed to 40°C for 1, 3, and 5 hours to determine optimal sublimation time.

Evaluation Parameters:
Pre-compression: Flow properties, bulk density.

Post-compression: Hardness, friability, disintegration time, wetting time, drug content uniformity, and dissolution studies.

Compatibility Studies:
DSC, XRD, and FTIR: To confirm no drug-excipient interactions.

Stability Studies:
Tablets were stored at 30±2°C/70±5% RH and 40±2°C/75±5% RH for 6 months.

RESULT AND ANALYSIS

Spectroscopic analysis:

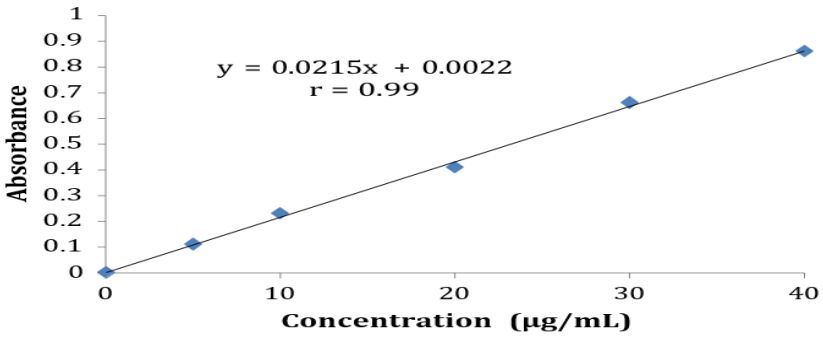


Fig.1 : Calibration curve for drotaverine HCl in 0.1N HCl

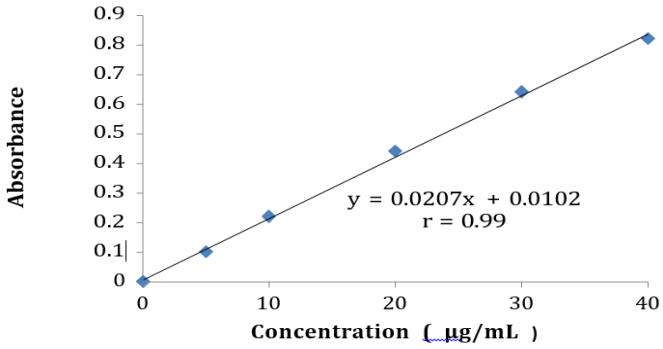
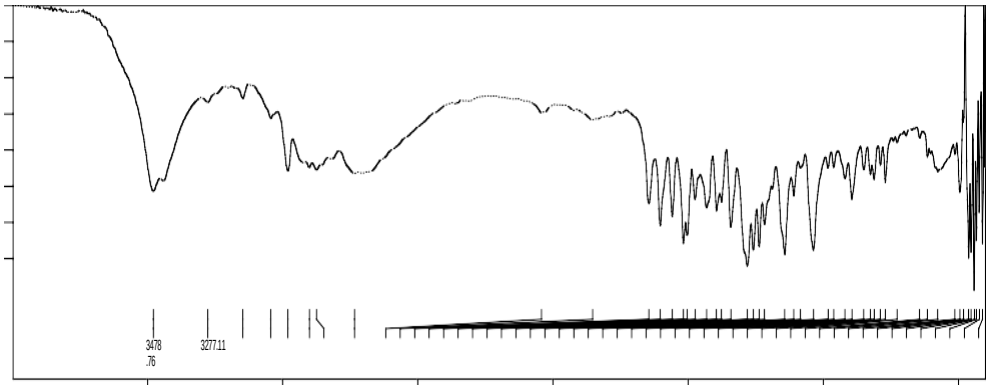


Fig.2 : Calibration Curve For Drotaverine Hcl In Ph 6.8 Phosphate Buffer



PRE COMPRESSION PARAMETERS

Evaluation of the granules:

Table 1 : Flow parameters for drotaverine HCl granules prepared using superdisintegrants

Formulation	Angle of repose (°)	Carr's index (%)	Hausner ratio
DX1	22.35	9.99	1.09
DX2	20.36	8.33	1.10
DX3	22.96	7.60	1.13
DY1	21.57	14.2	1.08
DY2	24.14	11.5	1.10
DY3	22.58	10.7	1.11
DZ1	21.52	13.7	1.15
DZ2	21.43	11.5	1.12
DZ3	20.28	7.6	1.08

Table2 : Flow Parameters For Drotaverine Hcl Granules Prepared Using Subliming Agents

Formulation	Angle of repose (°)	Carr's index (%)	Hausner ratio
DC1	21.52	8.33	1.08
DC2	20.35	7.4	1.12
DC3	22.96	9.09	1.09
DC4	21.57	14.2	1.08
DC5	23.15	11.5	1.10
DM1	23.15	10.7	1.12
DM2	20.28	13.7	1.15
DM3	21.43	11.5	1.13
DM4	22.35	7.6	1.08
DM5	20.46	9.09	1.10
DM6	23.33	8.33	1.09
DCM1	22.61	14.2	1.16
DCM2	23.45	11.5	1.13
DCM3	21.73	7.6	1.08
DCM4	20.76	10.7	1.12

Table 3: Percent of drug estimated in interference study

Excipient	%Drotaverine HCl (mean±s.d., n=3)
Camphor	100.13 ± 1.02
Menthol	99.29 ± 0.92
Mannitol	99.93 ± 0.38
Polyvinylpyrrolidone	99.75 ± 1.20
Talc	99.84 ± 0.84
Magnesium stearate	99.81 ± 1.02
Croscarmellose sodium	99.89 ± 1.28
Compritol 888 ATO	99.90 ± 1.72
Precirol ATO 5	100.1 ± 1.88
HPMC 3 cps	99.46 ± 1.96
Rxcipient FM1000	99.89 ± 1.54
Aspartame	100 ± 1.28
Sodium starch glycolate	99.98 ± 1.59
Crospovidone	99.77 ± 1.48

Table4 : Tabletting Properties of drotaverine HCl ODT (superdisintegrant evaluation)

Formulation code	Hardness (Kg/cm^2)	Friability (%)	t variation (mg)	Tablet thickness mm	*In vitro* disintegration time
DX1	2-3	0.52	101 ±1.45	3.10±1.02	90±0.90
DX2	2-3	0.50	100.5±1.20	3.12±1.22	76±1.00
DX3	2-3	0.48	97.5 ±1.35	3.14±1.10	30±1.32
DY1	2-3	0.47	104 ±1.60	3.12±1.14	80±0.80
DY2	2-3	0.46	101.5 ±1.20	3.10±1.12	62±0.10
DY3	2-3	0.36	101±1.45	3.14±1.24	45±1.26
DZ1	2-3	0.21	98.6±1.55	3.12±1.24	65±1.29
DZ2	2-3	0.25	100.4±1.64	3.10±1.16	39±1.43
DZ3	2-3	0.33	101±1.53	3.10±1.18	19±1.36

Table 5: Tabletting properties of drotaverine HCl ODT

Formulation code	Hardness (Kg/cm2)	Thickness (mm)	Friability (%)	Uniformity of weight (mg)	Uniformity of content(%)	*In vitro* disintegration time(Sec)	*In vitro* dispersion time(Sec)	*In vivo* disintegration time(Sec)	Wetting time(Sec)	Uniformity of dispersion
DC1	2.3	3.2	0.52	97	99.25	8.6	10	**6.5**	**6,5**	Pass
DC2	2.3	3.1	0.5	100.5	99.78	8.66	10	**5.4**	9.23	Pass
DC3	2.6	3.12	0.48	97.5	99.23	6.84	7	7.2	6.42	Pass
DC4	2.6	3.1	0.47	104	99.65	6.3	6	6.5	6.24	Pass
DC5	2.6	3.12	0.46	101.5	99.84	5.6	5	4.9	4.75	Pass
DM1	2.2	3.12	0.36	101	99.45	9.6	9	10.3	9.6	Pass
DM2	2.2	3.12	0.21	98.6	99.24	8.6	8	9.5	8.7	Pass
DM3	2.5	3.1	0.25	100.4	99.31	6.7	7	7.7	6.9	Pass
DM4	2.4	3.1	0.33	101	99.14	5.2	7	6.7	6.8	Pass
DM5	2.6	3.12	0.28	99.85	99.48	4.5	6	5.9	5.6	Pass
DM6	2.8	3.1	0.46	99.45	99.43	4.2	4	4	4.6	Pass
DCM1	2.5	3.14	0.36	99.5	99.59	8.7	8	7.7	8.2	Pass
DCM2	2.3	3.12	0.21	100.2	99.66	3.5	6	6.7	7	Pass
DCM3	2.4	3.1	0.25	98.8	99.74	4.2	5	4.9	5.3	Pass
DCM4	2.6	3.1	0.33	101	99.83	4	4	4.4	3.7	Pass

Table 6 : Effect of superdisintegrant concentration on disintegration of the tablet

Superdisintigrant	Crascarmelose sodium	Sodium starch glycolate	Avicil ph
2	65	80	90
3	39	62	76
4	19	45	30

Optimization of the sublimation time of exposure:

Table 7: Effect of sublimation time of exposure on disintegration time of the tablet

Superdisintegrant*	Before sublimation	Disintegration time (sec)		
		Sublimation time		
2	65	62	53	35
3	39	35	27	18.5
4	19	17	12	6.3

***In vitro* dissolution studies:**

Table 8: Cumulative percent drug released vs. time form drotaverine HCl ODT

Time (hr)	Cumulative % drug released							
	DC1	DC2	DC3	DC4	DC5	DM1	DM2	DM3
5	86.58	81.2	93.42	99	99.78	98.9	98. 8	77.28
10	87.07	83.64	98.8	101.7	102	99.8	100.8	100.2
15	88.53	84.62	100.1			100.1	100.8	100.2
30	89.51	85.11						
45	90	86.58						
60	90.49	87.55						
90	101.3	99.83						

	DM4	DM5	DM6	DCM1	DCM2	DCM3	DCM4
5	98.1	89.02	102.7	98.8	100.2	95.87	89.51
10	99.2	96.85	102.7	103.7	102.3	100.7	103.2
15	100.12	100.3	102.7	103.7	102.3	100.7	103.2

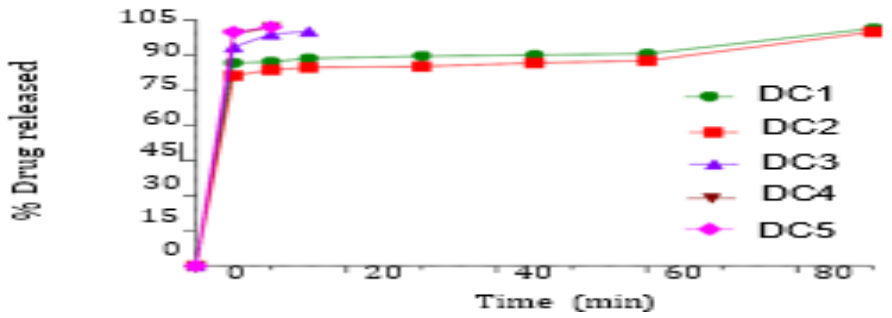


Fig3: Dissolution profile of the tablets prepared using camphor

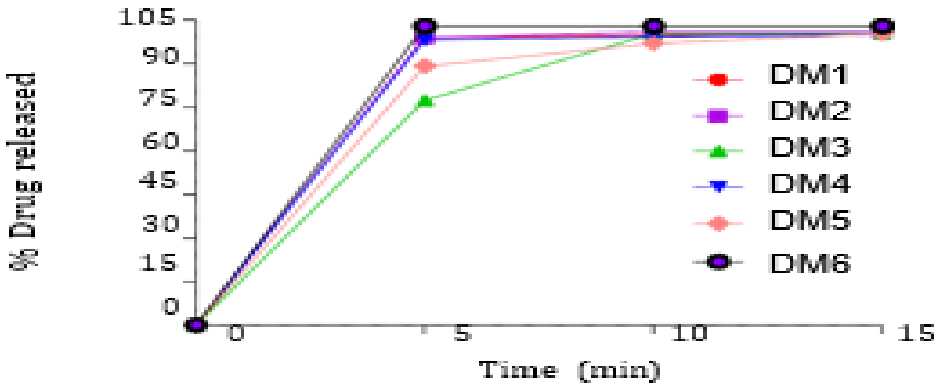


Fig.4: Dissolution profile of tablet prepared using menthol

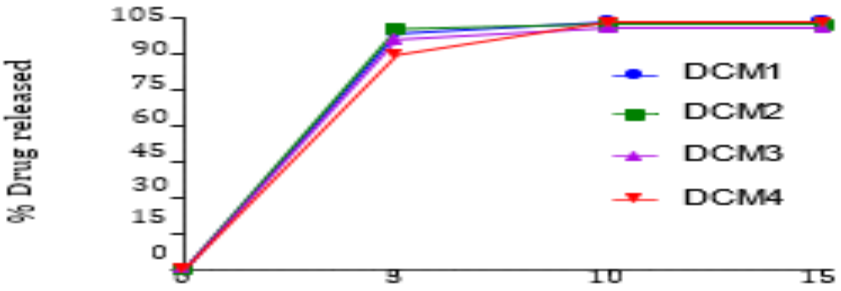


Fig5.: Dissolution profile of tablet prepared usingcamphor and mentholDrug-excipient cDSC analysis:

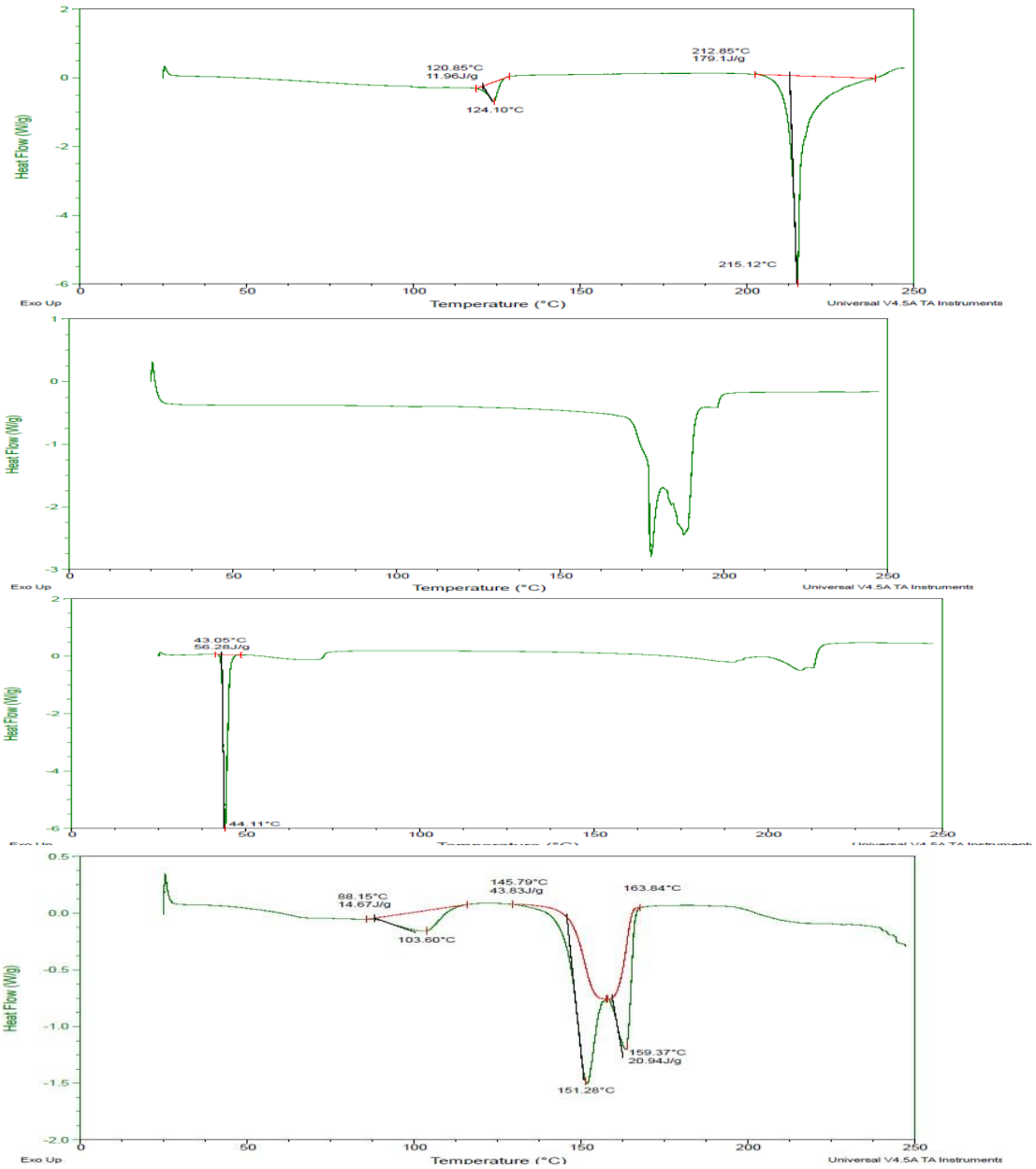


Fig.6 : DSC thermograms a) Drotaverine HCl, b) Camphor, c) Menthol and d) DCM2

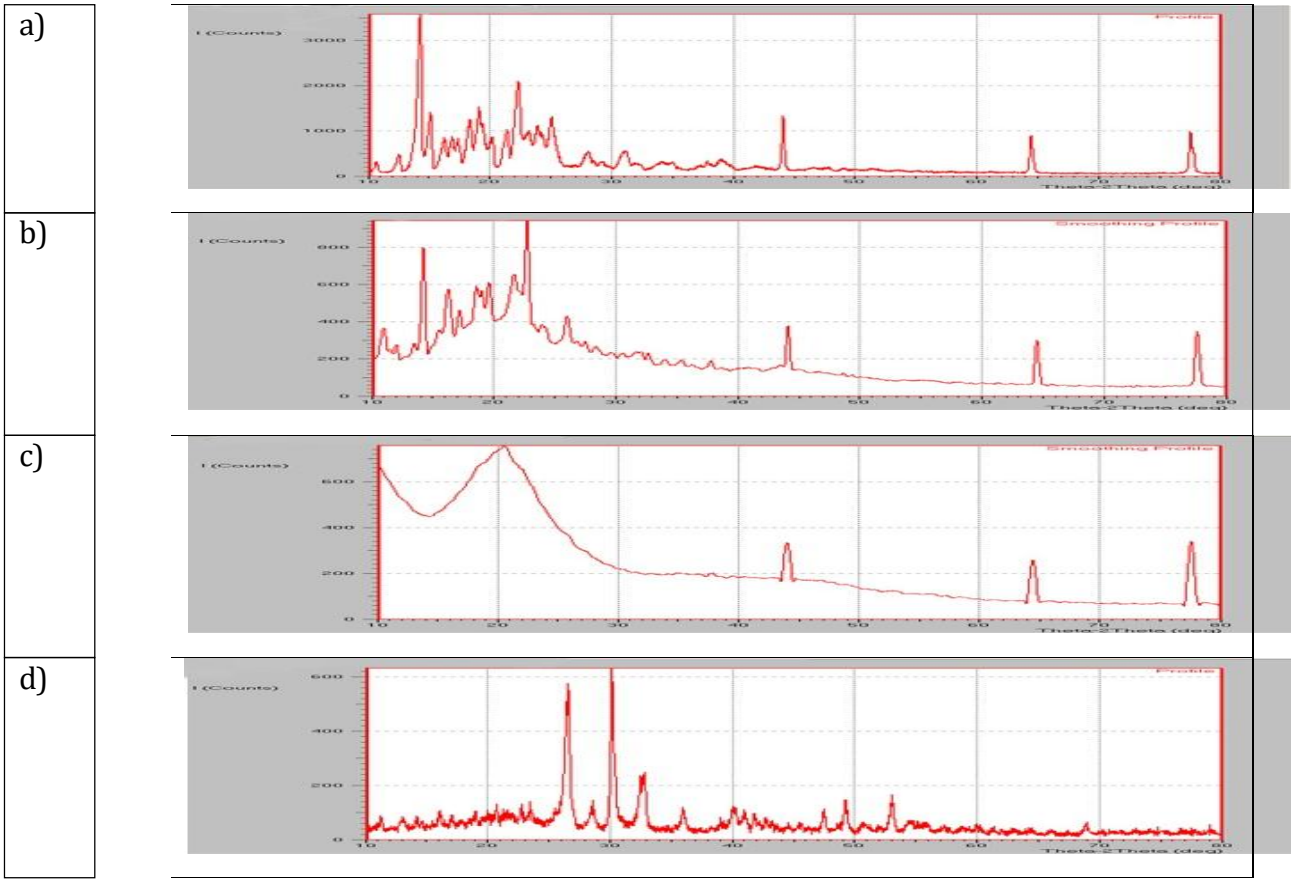


Fig.7 : X-ray diffractograms a) Drotaverine HCl, b) Camphor, c) Menthol and d) DCM2

STABILITY STUDIES OF THE OPTIMIZED FORMULATION

Table 9: Stability data of DCM2 Storage conditions

Test	Initial	30±2°C/70±5% RH		40±2°C/75±5% RH	
		3 months	6 months	3 months	6 months
Physical appearance	Pale yellow colour	Pale yellow colour	Pale yellow colour	Pale yellow colour	Pale yellow colour
Average weight* (mg)	100.2±1.47	101±0.12	101±0.23	102±0.97	101±0.77
content (%) Uniformity of drug	99.74±0.65	99.60±0.86	99.42±0.45	99.83 ±0.76	99.39 ±0.45
Hardness* (Kg/cm²)	2-3	2-3	2-3	2-3	2-3
Wetting time* (sec)	7.0±1.41	8.0±1.25	8.0±1.29	8.0±1.85	8.0±1.56

x: mean±% deviation (n=20) ; y: mean±s.d. (n=10); * n=6

Table10 : Cumulative % drug released from stability loaded ODT

Storage conditions					
Time (min)	Initial	30±2°C/70±5% RH		40±2°C/75±5% RH	
		3 months	6 months	3 months	6 months
			DCM2		
5	100.2± 1.21	99.4± 0.81	100 ± 1.25	100.4 ± 1.05	101.1 ± 1.25
10	102.3± 1.22	100 ± 1.32	101 ± 1.15	100.2 ± 0.99	100.24 ± 1.24
15	102.3± 1.81	100 ± 1.25	101 ± 1.14	100.68 ± 0.98	100.97 ± 1.14

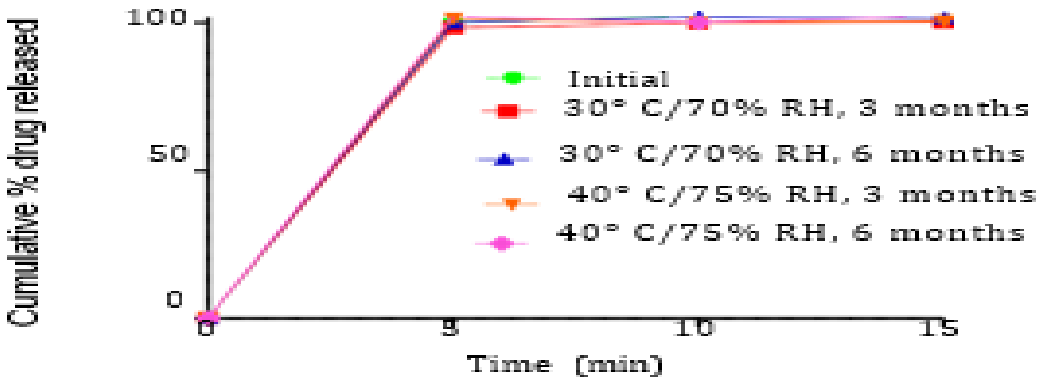


Fig 8: Comparative dissolution profiles of DCM2 before and after storage at 30±2° C/70±5% RH and 40±2° C/75±5% RH

CONCLUSION

The study successfully developed Drotaverine HCl ODTs with rapid disintegration and dissolution. Croscarmellose sodium (4%) and sublimation (5-hour exposure) were critical for optimal performance. Formulation DCM2, combining camphor and menthol, exhibited the fastest drug release (100.16% in 5 min) and stability under ICH guidelines. The results suggest that DCM2 is a promising ODT formulation for enhancing therapeutic efficacy and patient compliance. Future studies could explore scalability and in vivo performance.

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