RESEARCH PAPER

Formulation and Evaluation of Mouth Dissolving Tablets Containing Naproxen and Domperidone for Acute Migraine Management

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ABSTRACT

Background: Nausea, vomiting and gastric stasis accompanying migraine attacks impair swallowing and absorption of conventional oral analgesics. A fixed-dose combination of naproxen (NSAID) and domperidone (antiemetic–prokinetic) is clinically used, yet is available only as swallowable tablets.

Objective: To develop and evaluate mouth dissolving tablets (MDTs) of naproxen (250 mg) and domperidone (10 mg) by direct compression that disintegrate rapidly and release both drugs faster than the marketed conventional tablet.

Methods: Nine batches (F1–F9) were prepared using crospovidone, croscarmellose sodium or sodium starch glycolate at 2, 4 and 6 % w/w, with mannitol and microcrystalline cellulose as diluents. Blends and tablets were evaluated for pre- and post-compression parameters, wetting time, disintegration time (DT), drug content, in vitro dissolution (USP II, phosphate buffer pH 6.8) and accelerated stability (40 °C/75 % RH, 3 months). A validated simultaneous-equation UV method (271 and 285 nm) was used for assay and dissolution analysis.

Results: All batches met pharmacopoeial limits for weight variation, hardness (3.59–3.95 kg/cm²), friability (<1 %) and content uniformity. DT decreased with increasing superdisintegrant concentration in the order crospovidone < croscarmellose sodium < sodium starch glycolate (two-way ANOVA, $p < 0.0001$). Batch F3 (6 % crospovidone) showed the shortest DT (17.4 ± 1.5 s), released 82.6 % naproxen and 84.0 % domperidone in 10 min, followed first-order kinetics with anomalous transport ($n \approx 0.7$), and was significantly faster than the marketed tablet (similarity factor $f_2 < 50$). FTIR and DSC confirmed drug–excipient compatibility. F3 remained stable under accelerated conditions.

Conclusion: Direct-compression MDTs of naproxen and domperidone with 6 % crospovidone offer a patient-friendly, rapidly disintegrating alternative for early treatment of migraine with nausea.

Keywords: Mouth dissolving tablets; Orodispersible tablets; Naproxen; Domperidone; Crospovidone; Migraine; Direct compression; Superdisintegrant

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INTRODUCTION

The oral route remains the preferred mode of drug administration because of convenience, safety and cost-effectiveness. Nevertheless, conventional tablets and capsules present a significant barrier for patients with dysphagia, which affects roughly one-third of the general population, 30–40 % of elderly in-patients and 18–22 % of residents in long-term care 1,2. Children, bedridden patients and those experiencing nausea or vomiting are particularly disadvantaged. Mouth dissolving tablets (MDTs), also termed orally disintegrating or orodispersible tablets, were developed to overcome these limitations3–7. An MDT is placed on the tongue, disintegrates within seconds in saliva without water, and is swallowed as a fine suspension 8–10. Regulatory definitions require disintegration in approximately 30 s (US FDA guidance) or within 3 min (European Pharmacopoeia)11.

Migraine is a highly prevalent primary headache disorder that affects approximately 1.2 billion people worldwide and is a leading cause of disability, especially in women of working age12. Nausea is reported by about 73 % and vomiting by about 29 % of migraineurs; both symptoms reduce willingness to take oral medication and are compounded by delayed gastric emptying that slows absorption of analgesics13,14. Domperidone, a peripheral dopamine D_2-receptor antagonist, accelerates gastric emptying and controls nausea without significant central side effects15,16, while naproxen provides sustained analgesia through non-selective cyclo-oxygenase inhibition17. Fixed-dose combinations of naproxen (250 or 500 mg) with domperidone (10 mg) are widely

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prescribed in India for acute migraine, yet only conventional swallowable tablets are marketed18. Regulatory attention to cardiac safety has restricted the adult dose of domperidone to a maximum of 30 mg per day for up to 7 days19.

Although MDTs of naproxen sodium1,20,21 and of domperidone22–24 have been reported separately, no published work describes a combined MDT of the two drugs. The formulation challenge is substantial: naproxen is a high-dose (250 mg), poorly water-soluble weak acid (BCS Class II)17, whereas domperidone is a low-dose, bitter weak base with extensive first-pass metabolism15,16. The opposing pH-dependent solubilities and the need for rapid disintegration with adequate mechanical strength therefore require systematic optimisation of superdisintegrant type and concentration25–28. The present study aimed to formulate MDTs of naproxen and domperidone by direct compression9,29,30, compare three commonly used superdisintegrants (crospovidone, croscarmellose sodium and sodium starch glycolate) at three levels, select an optimised batch on the basis of disintegration time and drug release, and evaluate its stability and performance relative to a marketed conventional tablet.

MATERIALS AND METHODS

Materials

Naproxen and domperidone were obtained as gift samples of pharmaceutical grade. Crospovidone (Kollidon CL-SF), croscarmellose sodium (Ac-Di-Sol) and sodium starch glycolate (Primojel) were used as superdisintegrants25,26. Microcrystalline cellulose (Avicel PH 102) and directly compressible mannitol served as diluents. Aspartame, peppermint flavour, magnesium stearate and talc were of pharmaceutical grade. All solvents and reagents were of analytical or HPLC grade. A marketed conventional naproxen–domperidone tablet (naproxen 250 mg + domperidone 10 mg) was purchased from a local pharmacy and used as the reference product. Double-distilled water was used throughout.

Preformulation studies

Organoleptic properties, melting points (capillary method) and solubility of both drugs in water, 0.1 N HCl and phosphate buffers (pH 6.8 and 7.4) were determined. UV spectra were recorded and a simultaneous-equation method was developed for the estimation of naproxen (λmax 271 nm) and domperidone (λmax 285 nm) in phosphate buffer pH 6.818. The method was validated for linearity, accuracy (recovery), precision (intra- and inter-day) and limits of detection/quantitation according to ICH Q2(R1)31. Drug–excipient compatibility was assessed by Fourier-transform infrared (FTIR) spectroscopy (KBr pellet, 4000–400 cm^{-1}) and differential scanning calorimetry (DSC, 50–300 °C, 10 °C/min, nitrogen atmosphere) of pure drugs, physical mixtures and the optimised formulation1,22.

Formulation of mouth dissolving tablets

Nine batches (F1–F9) were prepared by direct compression according to a 3^2 design in which the type of superdisintegrant (crospovidone, croscarmellose sodium, sodium starch glycolate) and its concentration (2, 4, 6 % w/w) were the independent variables (Table 1)9,27,29. Each tablet contained 250 mg naproxen and 10 mg domperidone; the total tablet weight was 400 mg. Mannitol and microcrystalline cellulose were used as diluents, aspartame and flavour as sweetener and flavouring agents24, and magnesium stearate (1 %) and talc (1 %) as lubricant and glidant. The powders were passed through a #60 sieve, blended geometrically, lubricated and compressed on a rotary tablet machine fitted with 12 mm flat punches8,10.

Table 1. Composition of mouth dissolving tablet batches F1–F9 (mg per tablet)

Ingredient	F1	F2	F3	F4	F5	F6	F7	F8	F9
Naproxen	250	250	250	250	250	250	250	250	250
Domperidone	10	10	10	10	10	10	10	10	10
Crospovidone	8 (2%)	16 (4%)	24 (6%)	–	–	–	–	–	–
CCS	–	–	–	8 (2%)	16 (4%)	24 (6%)	–	–	–
SSG	–	–	–	–	–	–	8 (2%)	16 (4%)	24 (6%)
MCC + Mannitol	116	108	100	116	108	100	116	108	100
Aspartame + flavour	8	8	8	8	8	8	8	8	8
Mg stearate + talc	8	8	8	8	8	8	8	8	8
Total weight	400	400	400	400	400	400	400	400	400

CCS = croscarmellose sodium; SSG = sodium starch glycolate; MCC = microcrystalline cellulose. Levels in parentheses are % w/w. Aspartame + flavour = aspartame 6 mg + peppermint flavour 2 mg; Mg stearate + talc = 4 mg + 4 mg (1 % each); MCC + mannitol was adjusted to make up the total tablet weight of 400 mg.

Evaluation of powder blends and tablets

Pre-compression parameters (bulk and tapped density, Carr's index, Hausner ratio, angle of repose) were determined by standard methods3,5. Post-compression evaluation included weight variation (n = 20), thickness, hardness (Monsanto/digital tester, n = 6), friability (Roche friabilator, 25 rpm, 4 min), wetting time, in vitro disintegration time (USP basket-rack apparatus, water, 37 ± 0.5 °C, n = 6) and drug content by the validated simultaneous-equation method1,22,23.

In vitro dissolution and kinetic modelling

Dissolution was performed in USP Apparatus II (paddle) at 50 rpm in 900 mL phosphate buffer pH 6.8 at 37 ± 0.5 °C3,11. Samples withdrawn at predetermined intervals

were analysed by the simultaneous-equation method. Model-independent parameters were calculated from the release profiles: Q_{10} and Q_{30} (percentage of drug released at 10 and 30 min, respectively), T_{50} and T_{90} (time, in min, required for 50 % and 90 % of the drug to be released) and dissolution efficiency DE_{30}% (area under the dissolution curve up to 30 min expressed as a percentage of the area of the rectangle corresponding to 100 % release over the same period; $DE_{30}\% = [\int y\,dt / (y_{100} \times 30)] \times 100$, where y is the percentage of drug released at time t)32. The dissolution profile of the optimised batch (test) was compared with that of a marketed conventional tablet (reference) using the difference factor $f_1 = \{\Sigma|R_t - T_t| / \Sigma R_t\} \times 100$, which measures the percentage difference between the two profiles at each time point, and the similarity factor $f_2 = 50 \times \log\{[1 + (1/n)\Sigma(R_t - T_t)^2]^{-0.5} \times 100\}$, which measures the closeness of the two profiles (R_t and T_t = percentage released from the reference and test at time t; n = number of time points). Values of $f_1 > 15$ and $f_2 < 50$ indicate dissimilar profiles33. Release data of the optimised batch were fitted to zero-order, first-order, Higuchi, Korsmeyer–Peppas and Hixson–Crowell models34.

Statistical analysis and stability study

Two-way analysis of variance (ANOVA) with type and concentration of superdisintegrant as factors, post-hoc pairwise comparisons (Bonferroni-adjusted), linear regression and Pearson correlation were performed; $p < 0.05$ was considered significant29. The optimised batch was packed in aluminium–aluminium blisters and stored at 40 ± 2 °C / 75 ± 5 % RH for three months according to ICH Q1A(R2)35. Samples were evaluated for appearance, hardness, friability, disintegration time, drug content and Q_{10} (percentage of drug released at 10 min) at 0, 1, 2 and 3 months.

RESULTS AND DISCUSSION

Preformulation and analytical method

Naproxen and domperidone were white crystalline powders with melting points of 154–156 °C and 243–245 °C, respectively, consistent with literature values15,17. Naproxen exhibited higher solubility at pH 6.8, while domperidone was more soluble in acidic medium, reflecting their weak-acid and weak-base character15,17. Overlay UV spectra (Figure 1) justified the simultaneous-equation approach18. The method obeyed Beer–Lambert law over 5–30 µg/mL (calibration points 5, 10, 15, 20, 25 and 30 µg/mL) for naproxen ($y = 0.0368x + 0.0034$, $R^2 = 1.0000$) and over 2–12 µg/mL (2, 4, 6, 8, 10 and 12 µg/mL) for domperidone ($y = 0.0418x + 0.0048$, $R^2 = 0.9999$) (Figure 2). Mean recoveries were 99–101 % with %RSD < 1 %; intra- and inter-day precision %RSD values were below 1 %, meeting ICH Q2(R1) criteria31. LOD/LOQ were 0.164/0.496 µg/mL (naproxen) and 0.101/0.307 µg/mL (domperidone) (Table 2).

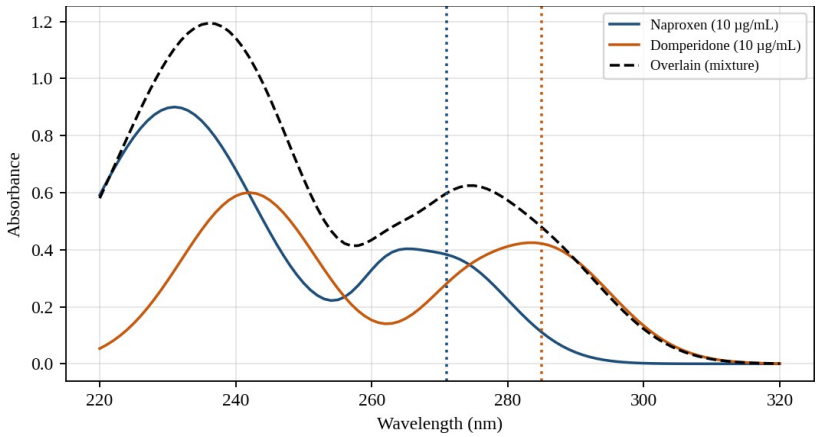


Figure 1. UV absorption spectra of naproxen (10 µg/mL), domperidone (10 µg/mL) and their mixture in phosphate buffer pH 6.8. Vertical lines mark analytical wavelengths (271 and 285 nm).

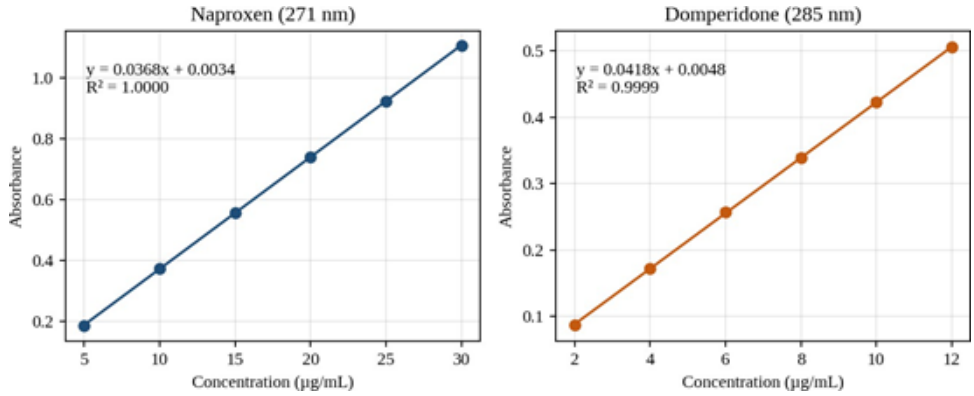


Figure 2. Calibration curves of naproxen (271 nm) and domperidone (285 nm) in phosphate buffer pH 6.8.

Table 2. Regression and validation parameters of the simultaneous-equation UV method

Parameter	Naproxen	Domperidone
λmax (nm)	271	285
Beer's law range (µg/mL)	5–30	2–12
Slope	0.0368	0.0418
Intercept	0.0034	0.0048
Correlation coefficient (R^2)	1.0000	0.9999
LOD (µg/mL)	0.164	0.101
LOQ (µg/mL)	0.496	0.307
Recovery (%)	99.69–100.36	99.50–101.31
Intra-day precision (%RSD)	0.64	0.72
Inter-day precision (%RSD)	0.88	0.97

Beer's law range = concentration range over which absorbance is directly proportional to concentration (calibration points as in Figure 2); LOD = limit of detection; LOQ = limit of quantitation; RSD = relative standard deviation.

FTIR spectra of the physical mixture and optimised formulation retained the characteristic bands of both drugs (carboxylic C=O of naproxen ≈ 1728 cm^{-1}; N–H and carbonyl of domperidone ≈ 3380 and 1713 cm^{-1}) with shifts < ±3 cm^{-1} and no new peaks, indicating absence of chemical interaction (Figure 3)1,22. DSC thermograms confirmed retention of the melting endotherms of naproxen (≈ 156 °C) and domperidone (≈ 245 °C) with only minor shifts attributable to dilution (Figure 4)1,17.

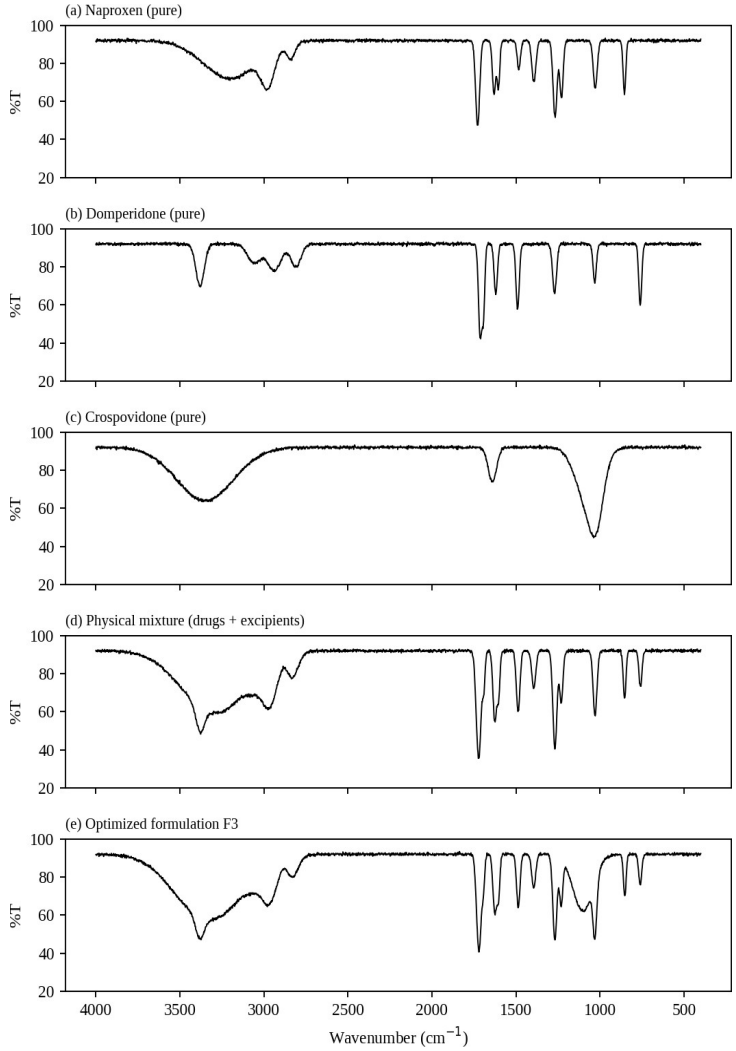


Figure 3. FTIR spectra of (a) naproxen, (b) domperidone, (c) crospovidone, (d) physical mixture of drugs with all excipients, and (e) optimised formulation F3.

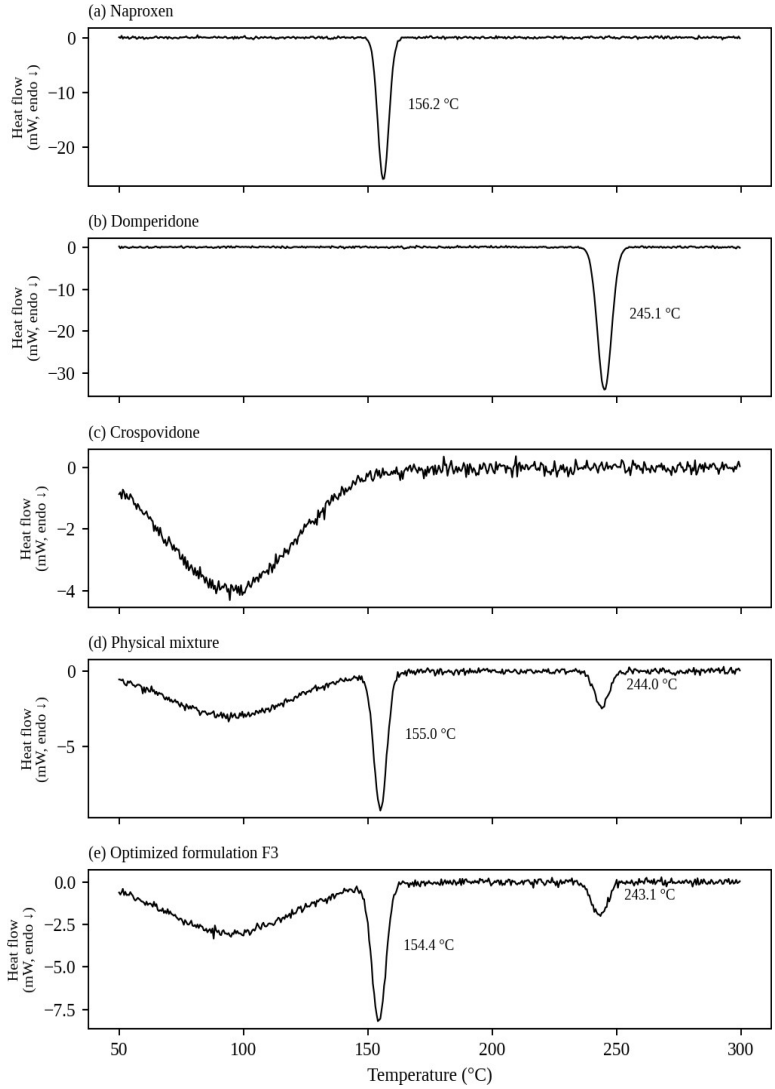


Figure 4. DSC thermograms of (a) naproxen, (b) domperidone, (c) crospovidone, (d) physical mixture, and (e) optimised formulation F3.

Pre-compression parameters

All nine blends exhibited good flow: Carr's index 10.8–15.0 %, Hausner ratio 1.12–1.18 and angle of repose 26.3–29.0° (Table 3), comparable to values reported for other direct-compression ODTs1,22,23. A modest increase in compressibility index and angle of repose was observed with higher superdisintegrant levels, particularly for croscarmellose sodium and sodium starch glycolate, consistent with their finer particle size and fibrous/hygroscopic nature25,26.

Crospovidone blends showed slightly better flow. The presence of directly compressible mannitol, Avicel PH 102 (coarse-grade microcrystalline cellulose) and talc contributed to the overall good flow, permitting uniform die filling without granulation3,9.

Table 3. Pre-compression parameters of powder blends (mean ± SD, n = 3)

Batch	Bulk density (g/mL)	Tapped density (g/mL)	Carr's index (%)	Hausner ratio	Angle of repose (°)
F1	0.500 ± 0.009	0.562 ± 0.005	10.93	1.12	26.3 ± 0.7
F2	0.500 ± 0.011	0.561 ± 0.008	10.75	1.12	26.6 ± 0.3
F3	0.477 ± 0.003	0.551 ± 0.005	13.42	1.16	26.6 ± 0.4
F4	0.521 ± 0.009	0.593 ± 0.005	12.13	1.14	26.9 ± 0.6
F5	0.501 ± 0.007	0.577 ± 0.008	13.31	1.15	27.4 ± 0.6
F6	0.487 ± 0.009	0.572 ± 0.009	14.98	1.18	28.6 ± 0.6
F7	0.536 ± 0.009	0.622 ± 0.010	13.89	1.16	27.6 ± 0.7
F8	0.512 ± 0.006	0.593 ± 0.006	13.59	1.16	28.2 ± 0.7
F9	0.504 ± 0.004	0.591 ± 0.010	14.77	1.17	29.0 ± 0.6

Post-compression parameters

All tablets were white, round, flat and free from defects. Average weights were 399.1–400.4 mg with maximum individual deviation ≤ 2.34 % (limit ±5 % for tablets > 324 mg). Thickness was uniform (4.15–4.23 mm). Hardness ranged from 3.59 to 3.95 kg/cm² and friability from 0.46 to 0.71 % (all < 1 %) (Figure 5, Table 4), within the range considered adequate for handling of MDTs1,3,5. A mild decrease in hardness and corresponding increase in friability accompanied rising superdisintegrant concentration, reflecting the elastic recovery and swelling tendency of the disintegrants25, yet all values remained within acceptable limits for handling.

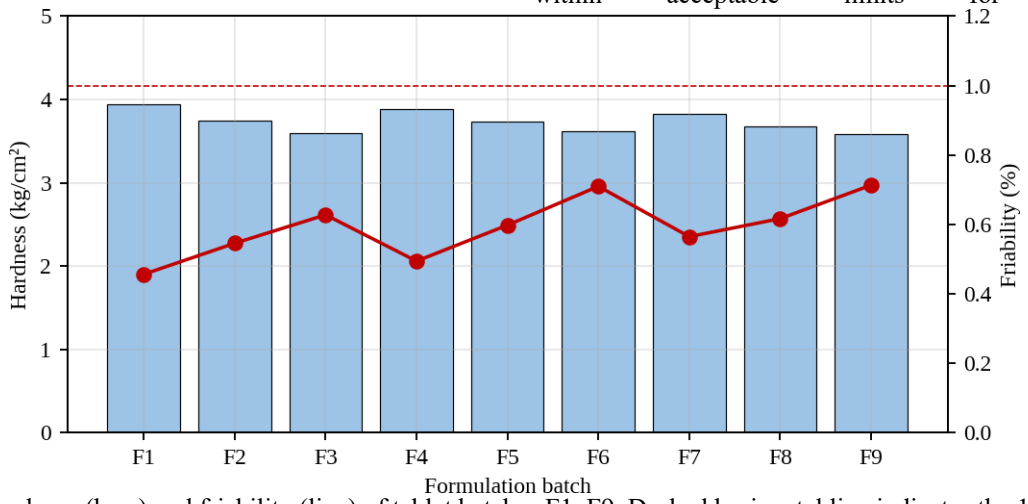


Figure 5. Hardness (bars) and friability (line) of tablet batches F1–F9. Dashed horizontal line indicates the 1 % friability limit.

Wetting time (22.6–56.2 s) improved with increasing superdisintegrant level (Figure 6). Crospovidone consistently produced the shortest wetting times, followed by croscarmellose sodium and sodium starch glycolate. This ranking is explained by the predominant capillary (wicking) action and lack of gel formation of crospovidone, whereas sodium starch glycolate acts mainly by swelling and may form a viscous barrier at higher levels25,26. In vitro disintegration time ranged from 17.4 ± 1.5 s (F3) to 51.4 ± 0.7 s (F7) (Figure 7). All batches complied with the European Pharmacopoeia limit of 3 min; batches F2, F3 and F6 also met the stricter FDA guidance of approximately 30 s11. Drug content of both actives was 97.9–100.5 % of label claim. These disintegration times are comparable to or faster than previously reported ODTs of the individual drugs1,20,22,23.

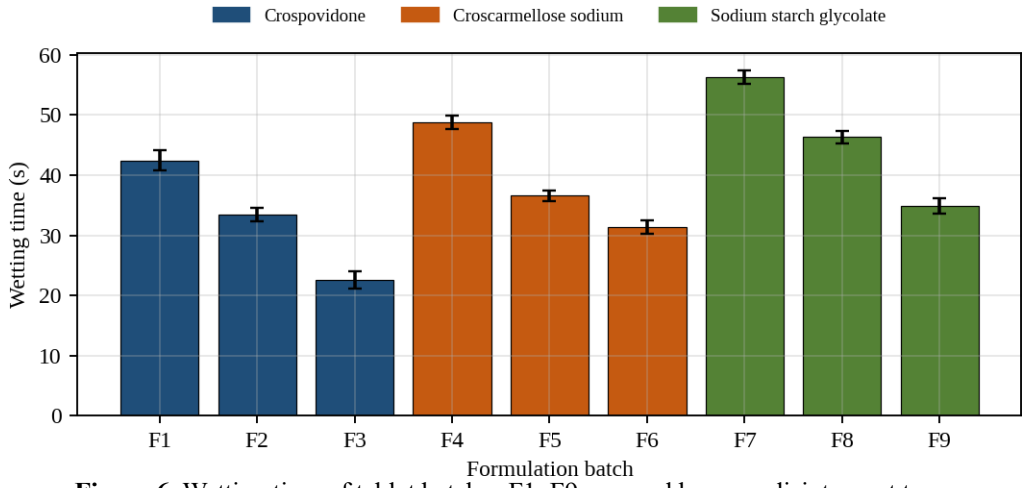


Figure 6. Wetting time of tablet batches F1–F9 grouped by superdisintegrant type.

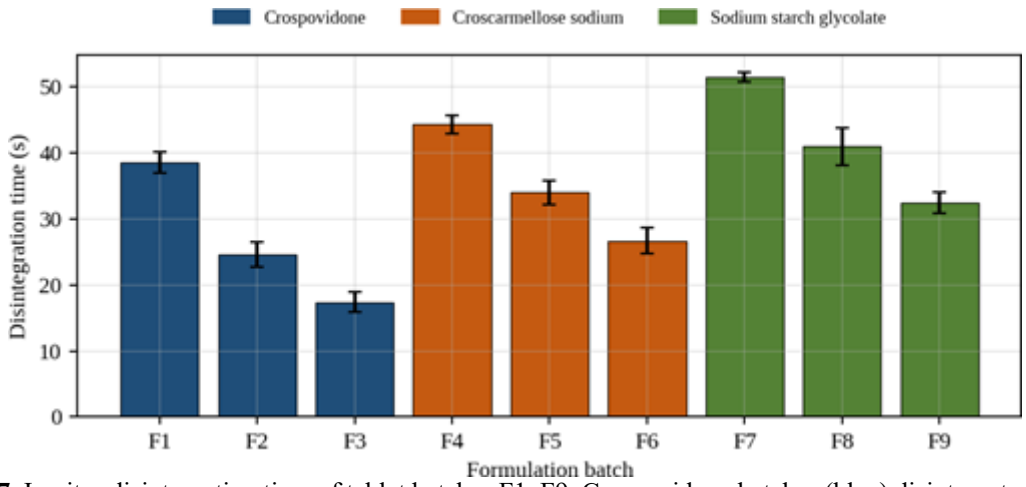


Figure 7. In vitro disintegration time of tablet batches F1–F9. Crospovidone batches (blue) disintegrated fastest.

Table 4. Key post-compression parameters of MDT batches (mean ± SD)

Batch	Hardness (kg/cm²)	Friability (%)	Wetting time (s)	DT (s)	NAP Q_{10} (%)	DOM Q_{10} (%)
F1	3.95 ± 0.17	0.46	42.4 ± 1.7	38.5 ± 1.6	66.9	71.4
F2	3.74 ± 0.24	0.55	33.5 ± 1.1	24.6 ± 1.9	77.3	78.7
F3*	3.59 ± 0.10	0.63	22.6 ± 1.5	17.4 ± 1.5	82.6	84.0
F4	3.88 ± 0.23	0.49	48.8 ± 1.1	44.3 ± 1.4	65.5	68.7
F5	3.73 ± 0.13	0.60	36.6 ± 0.9	34.0 ± 1.8	69.6	73.1
F6	3.62 ± 0.22	0.71	31.3 ± 1.1	26.7 ± 2.0	73.7	78.8
F7	3.83 ± 0.16	0.56	56.2 ± 1.1	51.4 ± 0.7	61.3	66.9
F8	3.68 ± 0.18	0.62	46.3 ± 1.0	40.9 ± 2.8	66.8	70.1
F9	3.59 ± 0.13	0.71	34.8 ± 1.3	32.5 ± 1.6	68.9	72.8

*Optimised batch (highlighted). DT = disintegration time; NAP = naproxen; DOM = domperidone; Q_{10} = percentage released at 10 min.

In vitro dissolution and kinetics

Release of both drugs increased with superdisintegrant concentration and followed the order crospovidone > croscarmellose sodium > sodium starch glycolate at each level (Figures 8 and 9), in agreement with comparative studies of superdisintegrant functionality22,25. After 10 min, naproxen release was 61.3–82.6 % and domperidone release 66.9–84.0 %. Batch F3 released 82.6 % naproxen and 84.0 % domperidone in 10 min and essentially complete amounts (98.3 % and 100.1 %) in 30 min. Strong inverse correlations between disintegration time and Q_{10} ($r = -0.973$ for naproxen, -0.977 for domperidone) confirm that disintegration is the rate-determining step for these poorly soluble BCS Class II drugs21,25.

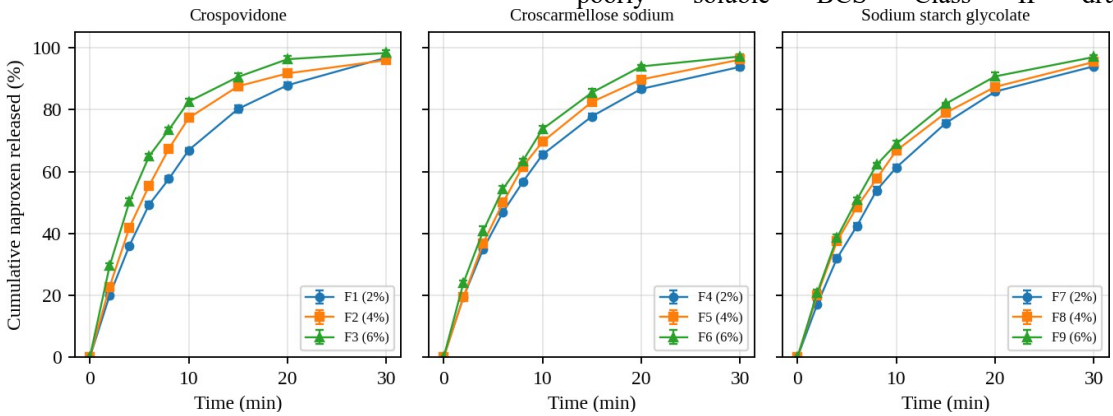


Figure 8. In vitro release profiles of naproxen from batches F1–F9 in phosphate buffer pH 6.8 (USP II, 50 rpm, 37 °C; mean ± SD, n = 3).

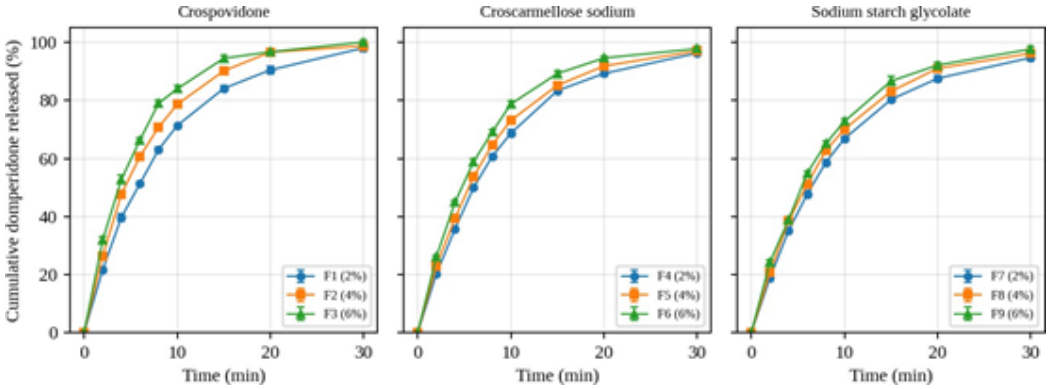


Figure 9. In vitro release profiles of domperidone from batches F1–F9 in phosphate buffer pH 6.8 (USP II, 50 rpm, 37 °C; mean ± SD, n = 3).

Kinetic modelling of F3 data showed the best fit to the first-order model (R^2 = 0.9808 naproxen, 0.9931 domperidone) and the Korsmeyer–Peppas model (R^2 = 0.9977 and 0.9959; release exponent n = 0.725 and 0.675) (Table 5)34. Values of n between 0.45 and 0.89 indicate anomalous (non-Fickian) transport, implying that release is controlled by a combination of tablet disintegration, particle wetting and drug dissolution/diffusion rather than pure diffusion34. Dissolution efficiency DE_{30}% reached 79.8 % (naproxen) and 81.8 % (domperidone) for F332.

Table 5. Kinetic modelling of drug release from optimised batch F3

Model	NAP R^2	NAP parameter	DOM R^2	DOM parameter
Zero-order	0.7159	k = 2.17	0.6963	k = 2.13
First-order	0.9808	k = 0.138 min^{-1}	0.9931	k = 0.189 min^{-1}
Higuchi	0.8593	k = 16.65	0.8434	k = 16.39
Korsmeyer–Peppas	0.9977	n = 0.725	0.9959	n = 0.675
Hixson–Crowell	0.9189	k = 0.105	0.9436	k = 0.119

Statistical analysis and selection of optimised batch

Two-way ANOVA demonstrated that both type (F = 312.3, p < 0.0001) and concentration (F = 535.0, p < 0.0001) of superdisintegrant exerted highly significant effects on disintegration time; concentration accounted for the larger share of variance (61 %). The interaction term was not significant (p = 0.0615). Pairwise comparisons confirmed crospovidone < croscarmellose sodium < sodium starch glycolate (all p < 0.05), consistent with mechanistic rankings reported previously22,25. Linear regression of DT on concentration yielded slopes of −5.28, −4.41 and −4.74 s per % for the three disintegrants (R^2 > 0.93). Batch F3 was the only formulation that simultaneously satisfied DT ≤ 30 s11, hardness 3–4 kg/cm², friability < 1 %, drug content 95–105 % and $Q_{10} \geq 80$ % for both drugs, and was therefore selected as optimised3,4,28.

Comparison with marketed tablet and stability

Under identical dissolution conditions the optimised MDT released 82.6 % naproxen and 84.0 % domperidone in 10 min, versus 42.3 % and 46.3 % from the marketed conventional tablet (Figure 10). Similarity factors were f_2 = 22.8 (naproxen) and 23.7 (domperidone), confirming dissimilar (and therapeutically desirable) faster release (Table 6)33. The difference factors (f_1 = 110.1 and 93.4) further support the substantial improvement in early-phase drug availability, which is clinically relevant given the importance of rapid onset in migraine with nausea13,14.

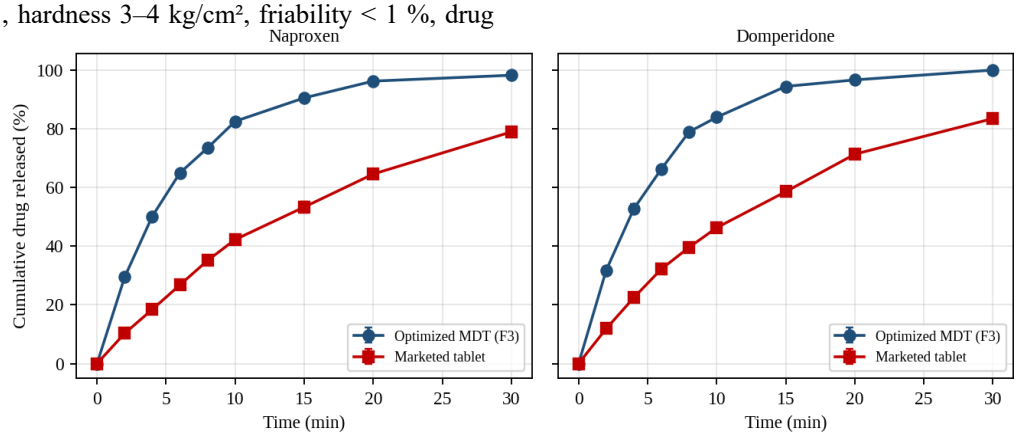


Figure 10. Comparative dissolution profiles of optimised batch F3 and the marketed conventional tablet of naproxen–domperidone (mean ± SD, n = 3).

Table 6. Comparison of dissolution parameters of F3 and the marketed tablet

Parameter	NAP – F3	NAP – Mkt	DOM – F3	DOM – Mkt
Q_{10} (%)	82.6	42.3	84.0	46.3
Q_{30} (%)	98.3	79.0	100.1	83.6
T_{50} (min)	4.0	12.6	3.6	11.2
T_{90} (min)	13.2	41.9	12.0	37.1
DE_{30} (%)	79.8	49.2	81.8	54.0
f_1 / f_2	—	110.1 / 22.8	—	93.4 / 23.7

Mkt = marketed conventional tablet; NAP = naproxen; DOM = domperidone; Q_{10} and Q_{30} = percentage of drug released at 10 and 30 min; T_{50} and T_{90} = time (min) for 50 % and 90 % of the drug to be released; DE_{30} = dissolution efficiency up to 30 min; f_1 = difference factor; f_2 = similarity factor ($f_1 > 15$ and $f_2 < 50$ indicate dissimilar profiles).

After three months at 40 °C/75 % RH, F3 showed no change in appearance; hardness decreased only marginally (3.59 → 3.47 kg/cm²), DT increased slightly (17.4 → 19.3 s), and drug content and Q_{10} remained within specification (content > 98 %, Q_{10} drop < 2 %) (Table 7, Figure 11), satisfying the criteria of ICH Q1A(R2)35. The minor changes are typical of moisture uptake by hygroscopic ODT excipients and underscore the necessity of aluminium–aluminium blister packaging3–5,27.

Table 7. Accelerated stability data of optimised batch F3 (40 ± 2 °C / 75 ± 5 % RH)

Parameter	0 month	1 month	2 months	3 months
Appearance	White, intact	No change	No change	No change
Hardness (kg/cm²)	3.59	3.54	3.50	3.47
Friability (%)	0.63	0.66	0.68	0.71
Disintegration time (s)	17.4	18.0	18.5	19.3
Naproxen content (%)	99.1	98.8	98.5	98.2
Domperidone content (%)	99.2	98.9	98.6	98.2
NAP released at 10 min (%)	82.6	82.2	81.7	81.1
DOM released at 10 min (%)	84.0	83.6	83.2	82.7

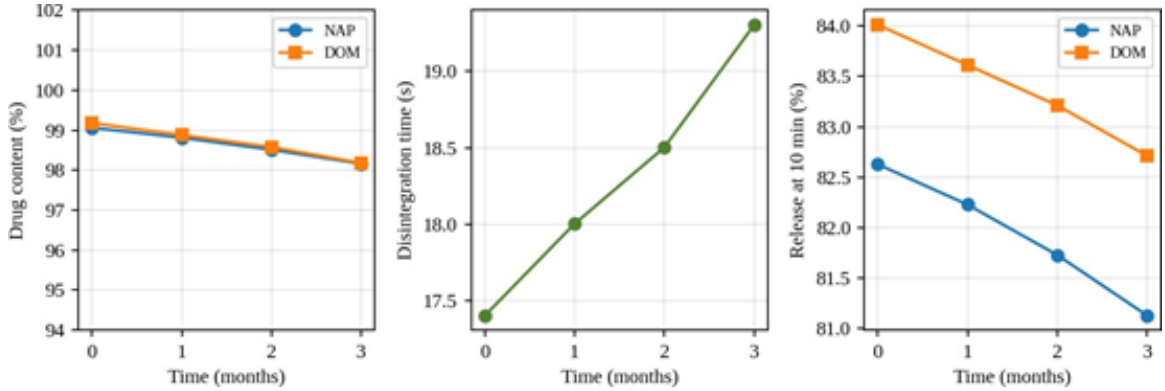


Figure 11. Effect of accelerated storage (40 °C / 75 % RH) on drug content, disintegration time and Q_{10} of optimised batch F3.

CONCLUSION

Mouth dissolving tablets containing 250 mg naproxen and 10 mg domperidone were successfully prepared by direct compression8–10. Both the type and the concentration of superdisintegrant significantly influenced wetting, disintegration and drug release25. Crospovidone at 6 % w/w (batch F3) produced the shortest disintegration time (17.4 s), the fastest release of both drugs (> 80 % in 10 min) and acceptable mechanical strength1,3,5. Release followed first-order kinetics with anomalous transport34. The optimised formulation dissolved significantly faster than a marketed conventional tablet33 and remained stable for three months under accelerated conditions35. The developed MDT offers a simple, scalable and patient-friendly alternative for the early treatment of migraine accompanied by nausea2,12–14, particularly for patients who have difficulty swallowing or lack ready access to water. Further in vivo pharmacokinetic studies are warranted to confirm the anticipated faster onset of action4,28.

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CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

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