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FORMULATION AND CHARACTERIZATION OF NAPROXEN AND SUMATRIPTAN BILAYER TABLETS

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ABSTRACT:

The present study was undertaken to formulate and evaluate bilayer tablets containing an immediate-release (IR) layer of Naproxen and a controlled-release (CR) layer of Sumatriptan to achieve rapid onset of analgesic action combined with sustained antimigraine activity. Nine formulations of Naproxen fast-dissolving tablets (IF1–IF9) and eight formulations of Sumatriptan controlled-release tablets (F1–F8) were developed using suitable superdisintegrants and hydrophilic matrix polymers, respectively. Pre-compression evaluation of both Naproxen and Sumatriptan granules indicated acceptable flow properties, with Carr's Index values ranging between 23–27% for Naproxen and 18–20% for Sumatriptan, and Hausner ratios within acceptable limits. These results confirmed that the granules were suitable for compression without significant flow-related challenges. All Naproxen fast-dissolving tablet formulations exhibited satisfactory post-compression characteristics. Hardness values (3.4–3.6 kg/cm²), friability (<1%), drug content (>98%), and uniform thickness demonstrated good mechanical stability. Disintegration time varied across formulations depending on the type and amount of superdisintegrant used. Formulation IF6, containing Crospovidone (15 mg), showed the shortest disintegration time of 72 seconds, indicating rapid tablet breakup and suitability for immediate drug release. Sumatriptan controlled-release formulations also showed acceptable post-compression performance, with hardness in the range 5.1–5.4 kg/cm², friability less than 1%, and uniform drug content. The use of HPMC grades (K4 and K15) in varying ratios effectively modulated drug release. Formulation F7 demonstrated optimal sustained-release

characteristics, releasing 99.25% of the drug at the 12-hour mark, thus meeting controlled-release expectations.

KEYWORDS: Formulation, Characterization, Naproxen, Sumatriptan, Bilayer Tablet, Migrain,

INTRODUCTION: MIGRAINE

Migraine is a highly disabling primary headache disorder with a 1-year prevalence of ~15% in the general population. According to the Global Burden of Disease Study, migraine is the second most prevalent neurological disorder worldwide and is responsible for more disability than all other neurological disorders combined (GBD, 2019). Migraine manifests clinically as recurrent attacks of headache with a range of accompanying symptoms. In approximately one third of individuals with migraine, headache is sometimes or always preceded or accompanied by transient neurological disturbances, referred to as migraine aura. Furthermore, a minority of those affected develop chronic migraine, in which attacks become highly frequent. The pathogenesis of migraine is widely believed to involve peripheral and central activation of the trigeminovascular system, and cortical spreading depression is thought to be the underlying neurophysiological substrate of migraine aura. However, much remains unknown about specific pathogenic processes and few mechanism-based treatment options currently exist (Natoli *et al*., 2010).

Migraine and the Brain:

As noted above, migraine probably results from adysfunction of brain-stem or diencephalic nuclei thatare involved in the sensory particularly nocicep-tive modulation of craniovascular afferents. Activation in the brain stem during attacks of migrainehas been detected with the use of positron-emission tomography. Moreover, the aura of migraine is likely to be the human counterpart of the animal phenomenon of L eao's spreading depression. Aurais characterized by a wave of oligemia that passes across the cortex at the characteristically slow rate of 2 to 6 mm per minute. A short phase of hyperemia precedes this oligemia and is likely to be a correlate of such symptoms as flashing, jagged lights. Oligemia is a response to depressed neuronal function and is still clearly present when the headache starts. These findings, together with direct evidence that the local oxygen supply is more than ad-equate, make the notion that migraine is simply a vascular headache untenable (Weiller *et al*., 1995).

Distinction between migraine and normal headache:

A headache is a pain in the head that occurs arbitrarily and at irregular intervals but is not actually a disease. The key difference between a migraine sufferer with pain and the pain of an ordinary headache is rather than the dull pain of a tension headache, 85 per cent of migraine sufferers experience a continual throbbing, pulsating or pounding pain which is felt with each beat of the heart, similar to a knife being stabbed continually into the head. As a consequence, migraines were thought to be caused by vasodilatation blood vessels in the brain expanding and pressing on pain-sensitive structures but experts are not sure what cause migraines. Migraines run in families, but it isn't clear why some people only get migraines out of them. Although term "migraine" is used to describe any severe headache, a migraine headache is the result of specific physiologic changes that occur within the brain (Olesen *et al*., 2009).

Literature Review: Das *et al*., (2025) Bilayer floating tablet of selected drug as Sucralfate and Metoprolol succinate. Sucralfate Immediate release layer containing Sucralfate100 mg and total weight with excipients is 300 mg. Metoprolol succinate sustained layer containing Metoprolol succinate 50 mg and total weight with excipients is 200 mg is done. Metoprolol succinate layer (MSF10) the (DSFMS-500mg) produce Average Weight 501.7±0.26 (mg), Thickness 5.99±0.111 mm, Hardness 5.6±0.124KP, Friability 0.543%, FLT 22 sec, TFT 18 hrs, Drug Content of Sucralfate 100.02%, Drug Content of Metoprolol Succinate is 99.98%. The TFT is under acceptance criteria (18-20hour).

Sandhra *et al*., (2024) reviewed on Sumatriptan succinate is an anti-migraine drug that is structurally similar to the serotonin and can induce the activation of 5HT receptor. Sumatriptan succinate is the first member of a new class of antimigraine compounds that act as a specific and selective 5-hydroxytryptamine-1 receptor agonist. Primarily due to presystemic first pass metabolism and partially due to inadequate absorption, sumatriptan succinate has a reduced bioavailability. Oral route of medication is a most favoured dosage form because of its simplicity of organization, non-obtrusiveness, flexibility, patient consistence and agreeableness. Advances in formulation technology have led to the development of various intraoral dosage forms and among them fast dissolving drug delivery systems (FDDDS) have gained popularity in recent years, the various types of polymers, the different methods for the preparation of fast dissolving films and evaluation tests for the oral films.

Nedeljkovi *et al.*, (2023) aimed to synthesized and investigated the dose-dependent antiinflammatory effect of new thiourea derivatives of naproxen with selected aromatic amines and esters of aromatic amino acids. The vivo study indicate that derivatives of m-anisidine (4) and N-methyl tryptophan methyl ester (7) showed the most potent anti-inflammatory activity four hours after injection of carrageenan, with the percentage of inhibition of 54.01% and 54.12%, respectively. In vitro assays of COX-2 inhibition demonstrated that none of the tested compounds achieved 50% inhibition at concentrations lower than 100 µM.

Simao *et al.*, (2023) reviewed that to established the basis for the implementation of Quality by Design (QbD) system principles for the design and development of bilayer tablets, encompassing the preliminary and systematic risk assessment of critical material attributes (CMAs) and critical process parameters (CPPs) with respect to in-process and finished product critical quality attributes (CQAs). Moreover, the applicability of the QbD methodology based on its purpose is discussed and complemented with examples of bilayer tablet technology.

Experimental Work and Result:

Determination of λ_{max} of Naproxen and Sumatriptan

The λ_{max} of Naproxen and Sumatriptan was determined by running the spectrum of drug solution in double beam ultraviolet spectrophotometer.

Procedure: Accurately weighed 10 mg of drugs was dissolved in 10 ml of 0.1 N HCl solutions in 10 ml of volumetric flask. The resulted solution 1000µg/ml and from this solution 0.1 ml pipette out and transfer into 10 ml volumetric flask and volume make up with 0.1 N HCl solution prepare suitable dilution to make it to a concentration of 10µg/ml for Naproxen and Sumatriptan. The spectrum of this solution was run in 200-400 nm range in U.V. spectrophotometer (Labindia-3000+). The spectrum peak point graphs of absorbance of Naproxen and Sumatriptan versus wave length were shown in figure 7.3-7.4.

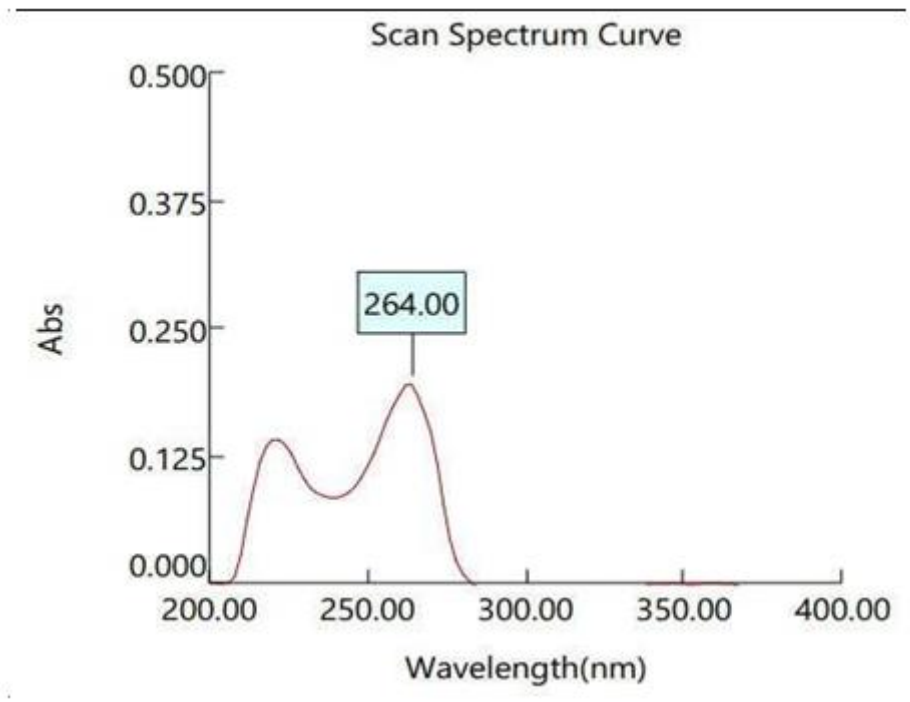

Figure 1: Determination of λ_{max} of Naproxen.

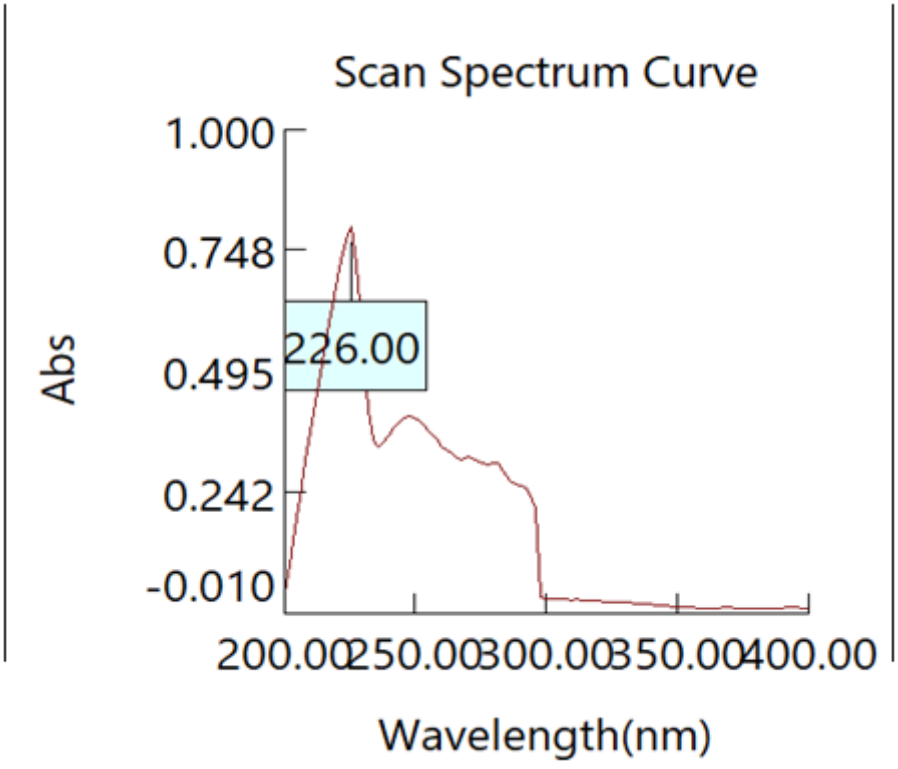

Figure 2: Determination of λ_{max} of Sumatriptan.

Calibration curve of Naproxen and Sumatriptan

Preparation of standard stock solution

10mg of drugs was weighed accurately and transferred to 10 ml volumetric flask, and the

volume was adjusted to the mark with the 0.1 N HCl to give a stock solution of 1000 ppm or µg/ml.

Preparation of working standard solution

From stock solutions of Naproxen1 ml was taken and diluted up to 10 ml. from this solution 0.2, 0.4, 0.6, 0.8 and 1.0 ml solutions were transferred to 10ml volumetric flasks and make up the volume up to 10 ml with 0.1 N HCl, gives standard drug solution of 2, 4, 6, 8, 10µg/ml concentration.

From stock solutions of Sumatriptan 1 ml was taken and diluted up to 10 ml. from this solution 0.2, 0.4, 0.6, 0.8 and 1.0 ml solutions were transferred to 10ml volumetric flasks and make up the volume up to 10 ml with 0.1 N HCl, gives standard drug solution of 2, 4, 6, 8, 10µg/ml concentration.

Calibration curve of Naproxen and Sumatriptan

Table 1: Readings for Calibration curve of Naproxen.

S. No.	Concentration (µg/ml)	Mean absorbance
1	2	0.179
2	4	0.332
3	6	0.463
4	8	0.615
5	10	0.767

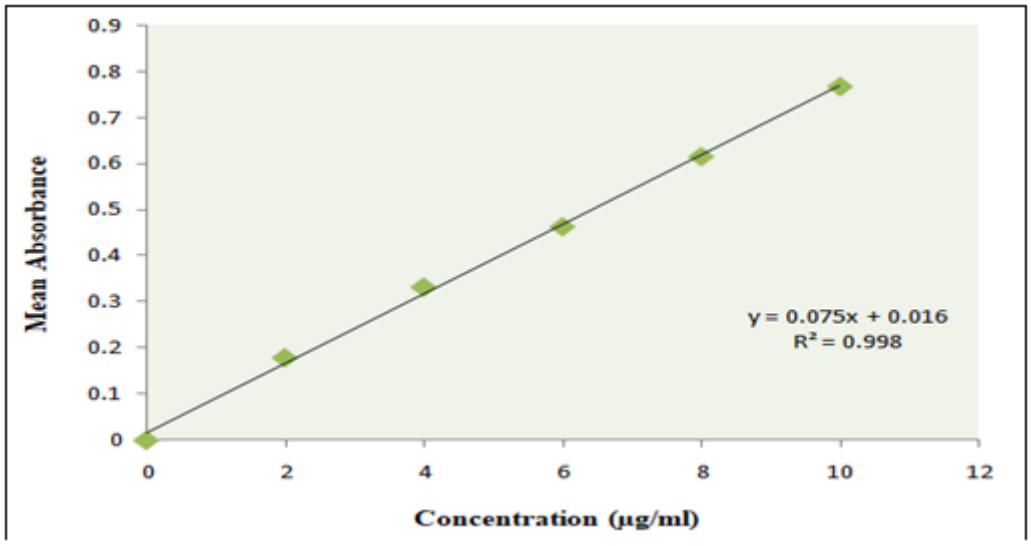

Figure 3: Calibration curve of Naproxen.

Table 2: Readings for calibration curve of Naproxen.

S. No.	Parameter	Results of Naproxen
1	Linearty range	2-10
2	Regression equation	y = 0.075x + 0.016
3	Correlation cofficient	0.998

Table 3: Readings for calibration curve of Sumatriptan.

S. No.	Concentration (µg/ml)	Mean absorbance
1	2	0.163
2	4	0.317
3	6	0.482
4	8	0.665
5	10	0.814

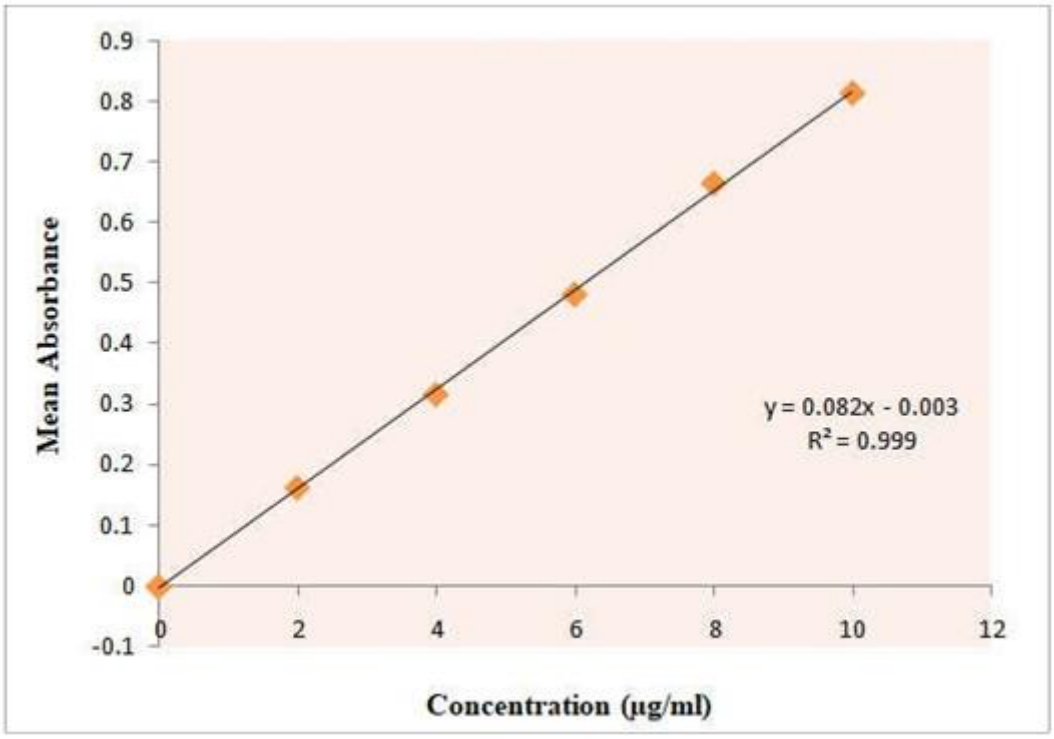

Figure 4: Calibration curve of Sumatriptan

Table 4: Stastical data for linearty

S.No.	Parameter	Results of Sumatriptan
1	Linearty range	2-10
2	Regression equation	y = 0.082x - 0.003
3	Correlation cofficient	0.999

CONCLUSION:

The preformulation studies of Naproxen and Sumatriptan were carried out to evaluate their fundamental physicochemical characteristics essential for designing a stable and effective bilayer tablet. The physical evaluation revealed that both drugs are white to off-white, odorless, and bitter-tasting crystalline powders. These sensory and physical characteristics are in accordance with pharmacopeial standards and indicate that both drug substances are suitable for solid oral dosage form development.

Solubility studies demonstrated distinct solubility profiles for the two drugs. Naproxen was slightly soluble in distilled water but showed good solubility in ethanol, methanol, chloroform, and buffer solutions of various pH conditions. In contrast, Sumatriptan was freely soluble in water and exhibited good solubility in acidic, alkaline, and phosphate buffer systems, although only sparingly soluble in ethanol and methanol. These findings highlight the pH-dependent solubility of both drugs and help in predicting their dissolution behavior in gastrointestinal conditions.

Thermal characterization through melting point determination showed sharp melting ranges for Naproxen (152–155°C) and Sumatriptan (169–170°C), confirming their purity and absence of polymorphic changes. The FT-IR spectra of both drugs displayed characteristic peaks corresponding to their functional groups without any unexpected peaks, thereby confirming their identity and chemical stability. These spectra serve as essential benchmarks for future compatibility and stability studies involving excipients.

Moisture content analysis through loss on drying revealed very low values for Naproxen (0.236 ± 0.001%) and Sumatriptan (0.184 ± 0.004%), indicating minimal hygroscopicity and good physical stability. This low moisture content is beneficial for tablet compression and reduces the risk of degradation during storage or processing.

UV spectrophotometric analysis further supported the analytical suitability of both drugs. The calibration curves constructed in the concentration range of 2–10 µg/ml showed excellent linearity, with correlation coefficients of 0.998 for Naproxen and 0.999 for Sumatriptan. The regression equations obtained confirm the accuracy and reliability of the developed UV method for quantitative estimation of both drugs in formulations.

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