Naproxen - An Anti-Inflammatory Agent - A Complete Pharmacokinetics, Pharmacodynamics and Comparative Study of Naproxen Sodium Tablet

Pranjal Shrichand Pawar[1], Vaishnavi Raju Bawne[2], Shankar Bhagawan khokle[3], Trupti Amod Raut[4], Avinash S. Jiddewar[5]

[1,2,3,5]*N S P M College of Pharmacy, Darwha, Dist-Yawatmal, India*

[4]*Assistant Professor in Department of Pharmacognosy and Phytochemistry at, N.S.P.M. College of Pharmacy, Darwha, Dist-Yavatmal, India*

***Abstract*— steroidal Anti-inflammatory Drugs (NSAIDs) are the main therapeutic alternatives in treating pain and inflammation among various populations. However, they are linked with some adverse reactions and drug interactions. This review aims to summarize the naproxen mechanism of action, pharmacokinetic and pharmacodynamic with comparative study of naproxen sodium tablet and place it in the therapeutic strategy. Naproxen is a reversible inhibitor of the pro-inflammatory enzyme cyclooxygenase (COX) used in clinical practice for control of pain of various origin, namely post-traumatic pain (distortion and sprain), post-operative pains (in traumatology, orthopedics, gynecology, maxillofacial surgery), gynecological pains (pain and discomfort at primary dysmenorrhea, after the introduction of an intrauterine coil, etc.), headache and toothache, prevention or treatment of migraine, spinal pains, extrarticular rheumatism.**

The objective of the present study is to develop a pharmaceutically stable and robust formulation of Naproxen sodium tablets USP 220mg comparable with innovator. In the present study we are reducing the excipients there by we can reduce the cost of the dosage form. The tablets of Naproxen sodium USP 220mg were successfully prepared by using wet granulation technique. Several trial formulations i.e., from F1-F10 have been taken to optimize and develop a robust formulation. The tablets were evaluated for weight variation, hardness, thickness, friability, % drug content, disintegration time and in vitro drug release. Formulation F10 showed a drug release of 103.5% in 60mins which is faster than the innovator product. The stability studies, shown that the formulation F10, F11 and F12 were stable enough at 400°C / 75% RH for a period of 3 months. Therefore, it can be concluded that the formulation F10 (Naproxen sodium tablets USP220mg) is robust and stable.

***Index Terms*— Cyclooxygenase (COX), Gastrointestinal (GI), Non-steriodal anti-inflammatory drugs (NSAID), Over -the- counter (OTC), Polyvinylpyrrolidone K-30 (PVP K- 30), Relative humidity (RH), Rapid mixer granulator (RMG), United States pharmacopoeia (USP).**

I. INTRODUCTION

Naproxen is an analgesic, antipyretic and non-steroidal anti-inflammatory drug (NSAID). It is a chemical category of naproxen is propionic acid derivative. Naproxen sodium is a white to creamy crystalline powder that has odourless. It is soluble in methanol and water. Naproxen has a molecular weight of 252.24 g/mol and melts at 105°C Manivannan et al; 2010 [15].

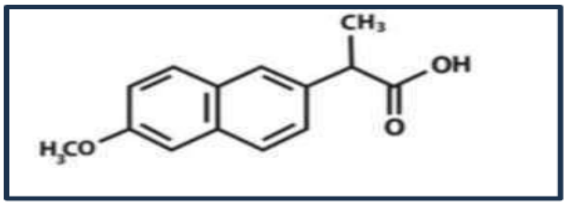
Naproxen was first authorized for prescription use in 1976 and remained so until 1994, when it was approved as an over-the-counter (OTC) drug. Naproxen has been FDA-approved to treat acute gout, ankylosing spondylitis, bursitis, polyarticular juvenile idiopathic arthritis, osteoarthritis, tendonitis, rheumatoid arthritis, pain, and primary Dysmenorrhea Joseph et al; 2025 [8]. At the same time, drugs labeled as "deliverance" from febrile conditions, pain syndrome, and rheumatologic complaints have been identified as one of the leading causes of hospitalization due to adverse drug reactions. Irrational NSAID administration has been linked to more deaths in Europe than traffic accidents or cancer, according to statistics. Considering the ongoing trend of more patients requiring anti- inflammatory therapy, selecting a nonsteroidal medication that is both safe and effective is essential Svetoslav et al; 2021 [20].

1.1 History

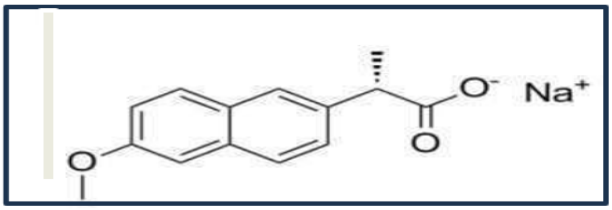
Further advances led to development of a new formulation of naproxen. Naproxen is a weak acid (pKa=4.15) with pharmacokinetics that limit the rate of absorption in the highly acidic environment of the gastrointestinal (GI) tract; adding an alkali salt improves absorption. Naproxen sodium it has been demonstrated that the formulation reaches the peak therapeutic index. more rapidly than naproxen (P < 01), had a significantly increased focus during the first two hours (P<.01), 24 and was approved by the FDA in 1981.25. Naproxen sodium was still only available with a prescription in the US until an over-the-counter medication was authorized by the FDA and duration in 1994, backed by data on safety and effectiveness for self-control Steven et al;

1.2 Mechanism Of Action

Naproxen has analgesic and anti-inflammatory properties by competitively inhibiting both cyclooxygenase (COX) isoenzymes, COX-1 and COX-2, by blocking arachidonate binding. The conversion of arachidonic acid to prostaglandin G (PGG), the initial stage of the synthesis of prostaglandins and thromboxanes involved in quick physiological reactions, is catalyzed by COX-1 and COX-2. While COX-2 is only expressed in the brain, kidney, bones, reproductive organs, and certain tumors like prostate and colon cancers, COX-1 is constitutively expressed in the majority of tissues. In addition to preserving normal renal function, gastric mucosal integrity, and hemostasis, COX-1 is in charge of prostaglandin synthesis in response to stimulation by circulating hormones. Many cells have the ability to produce COX-2 in response to particular inflammatory mediators, such as lipopolysaccharide, interleukin-1, and tumor necrosis factor B Joseph et al; 2025 [8].



STRUCTURE OF NAPROXEN
MOLECULAR FORMULA - $C_{14}H_{14}O_3$
Fig no.1



STRUCTURE OF NAPROXEN SODIUM
MOLECULAR FORMULA - $C_{14}H_{14}O_3$
Fig no.2

1.3 Advntages and Disadvantages of Naproxen

Advantages:

- Effective anti-inflammatory and analgesic action [23].
- Long duration of action and good tolerability [1,23].
- Efficacy similar to ibuprofen or diclofenac in reducing pain and inflammation [20].
- Reduces fever along with pain and inflammation [7].

Disadvantages:

- Causes nausea, heartburn,ulcers and bleeding due to COX-1 inhibition [6].
- Can cause elevated liver enzymes and rare liver injury [15].
- Rash,urticaria , or bronchospasm in aspirin-sensitive patients [12].
- Inhibites platelet aggregation and increasing bleeding tendency. [25].

II. PHARMACOKINETICS AND PHARMACODYNAMICS OF NAPROXEN

Table: 1 Pharmacokinatics

Bioavailability	95% (by mouth)
Protein binding	99%
Metabolism	Liver
Onset of action	1 hour
Elimination half- life	12–17 hours (adults)
Duration of action	12 hours
Excretion	Kidney

The oral nonsteroidal anti-inflammatory drug naproxen is quickly and fully absorbed, forms a strong bond with plasma albumin, and undergoes metabolism to produce glucuronide conjugates and sulfate metabolites that are eliminated in the urine. Its pharmacodynamics include reducing prostaglandin synthesis and inhibiting cyclooxygenase (COX) enzymes, which alleviates inflammation and pain. The oral nonsteroidal anti-inflammatory drug naproxen is quickly and fully absorbed, forms a strong bond with plasma albumin, and undergoes metabolism to produce glucuronide conjugates and sulfate metabolites that are eliminated in the urine. Its pharmacodynamics include reducing prostaglandin synthesis and inhibiting cyclooxygenase (COX) enzymes, which alleviates inflammation and pain.

III. PHARMACOKINETICS

Absorption: Complete and quick following oral administration.

Distribution: Extensively and concentration-dependently binds to plasma albumin. Glucuronide conjugates and sulfate metabolites are the main products of metabolism the liver

Excretion: Mainly eliminated in the urine, though a tiny quantity is expelled unaltered.

IV. PHARMACODYNAMICS

A nonsteroidal anti-inflammatory medication with standard pharmacodynamic characteristics is naproxen. It is more effective than aspirin and phenylbutazone because of its dose-related anti-inflammatory, analgesic, and antipyretic properties. Animals with adrenalectomy still exhibit its anti-inflammatory effects, suggesting a nonsteroidal mode of action. It is believed that naproxen's anti-inflammatory properties stem from its inhibition of cyclo-oxygenase, which lowers the levels of prostaglandin in different fluids and tissues.

Although it may cause endoscopically confirmed gastrointestinal lesions and gastrointestinal microbleeding, clinical practice indicates that naproxen and other NSAIDs are not significantly different in terms of tolerability. Although naproxen has little effect on human bleeding time, it is a strong inhibitor of the secondary phase of platelet aggregation.

It doesn't have any uricosuric properties. Naproxen can prevent bone and cartilage erosion in animals with adjuvant-induced arthritis, but it has no effect on collagen metabolism in healthy animals. Leucocyte function is impacted by naproxen, which lowers lysosomal and neutral protease, collagenase, and chemotaxis in animals K.D.Tripathi et al;[21],[22].

V. COMPARATIVE STUDY OF NAPROXEN SODIUM TABLET

Formulation of naproxen sodium tablet USP

Tablets of naproxen sodium with 220 mg were made using the wet granulation method and Table 3 displays the formulas used in the study. Naproxen is loaded during formulation F1, F2, and F3. adding sodium to the Rapid Mixer Granulator (RMG) Hyderabad's Boilers & Pneumatics) in addition to diluent (sodium starch glycolate, pregelatinized maize starch, and maize starch) and stirred for five minutes at slow speed of the mixer. PVP K-30 should be dissolved in hot water that has been purified.

Binder should be added to RMG while mixing with a slow mixer speed.

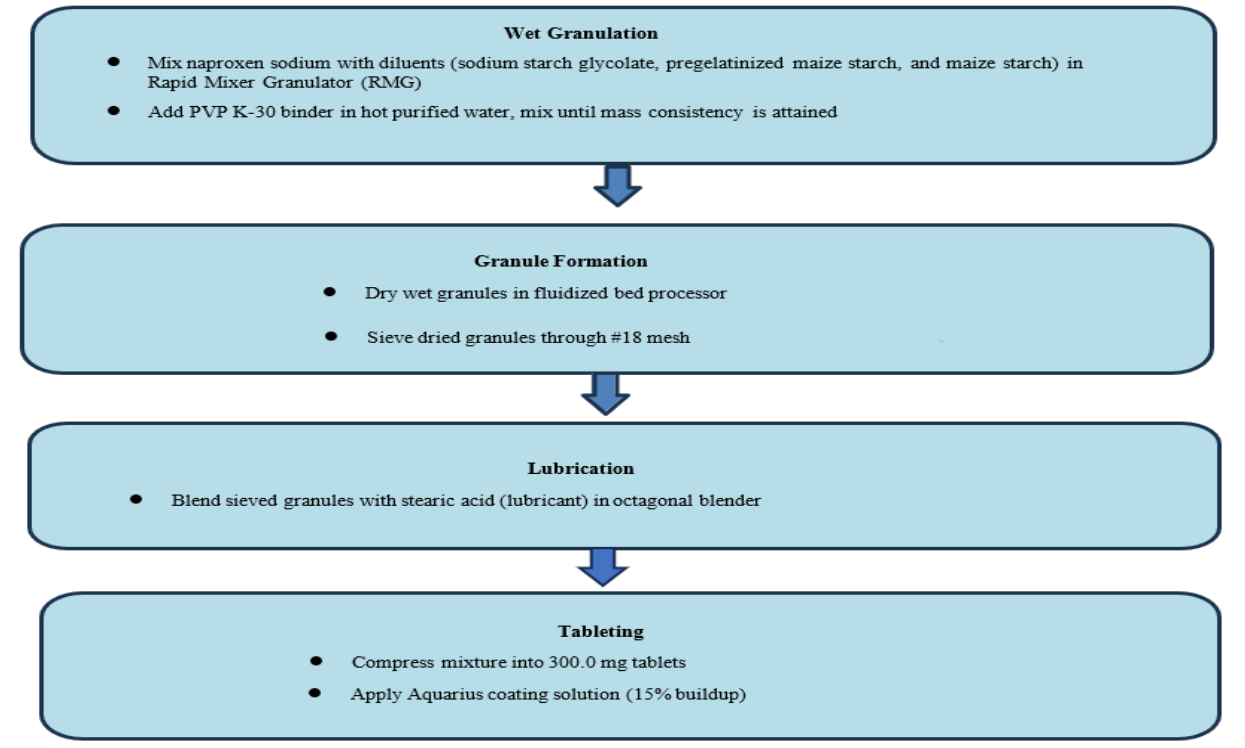
Add more water until the necessary mass consistency is attained. Granules were absent from Formulations F1 and F2. Better Granules during Formulation F3 were discovered, but DT wasn't compatible with the innovator. While F4, F5, F6, F7, F8, F9, and F10 maize formulations in place of starch, microcrystalline cellulose was used. Fill RMG with naproxen sodium and diluent (pregelatinized microcrystalline cellulose) sodium starch glycolate, maize starch, and a combination at low mixer speed for five minutes. Get rid of the PVP K-30 in heated, purified water. Binder should be added to RMG while using a slow mixer speed for mixing.

Set the process parameters and start the fluidized bed processor (Palm Glatt, Mumbai) in manual mode.as stated below. Dry the granules that are wet. Sort the dried through #18 mesh granules. Put the sieved into an octagonal blender (Saan, Mumbai) with granules. In a blender, stearic acid (lubricant) is added by blending for five minutes at eight rpm after sifting it through 40 mesh.

Compress the mixture into 300.0 mg tablets. Apply 15% to the tablets to achieve a 2.5% buildup. Aquarius coating solution BP 17066. While better granules were discovered in formulations F4 and F5, but Time of

disintegration does not correspond to the reference example. Formulations F6, F7, F8, and F9 Although the disintegration time was adequate, the percentage drug release compared to innovator's was lower example. Granules generated the course of Formulation F10 possess favorable profile matched sample of innovators. Two batches of reproducibility (F11) Formulation F10's & F12) were taken. Physical The granules' characteristics are comparable to those of F10. and both the chemical and the dissolution profiles. The tablets' characteristics are identical to those of the F10 Manivannon et al; 2010 [15].

Flow chart for the formulation of naproxen sodium tablets:



Formulation Process:

Formulation Variations:

- F1-F3: Used starch as diluent, granules absent in F1 and F2, F3 had better granules but incompatible disintegration time.
- F4-F10: Used microcrystalline cellulose instead of starch
- F10: Favorable profile matching innovator's sample
- F11 and F12: Reproducibility batches with similar physical and chemical characteristics to F10

Table: 2 Shows various Formulations of Naproxen Sodium Tablets USP

Ingredi ents (gms/ batch)	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10
Naproxen Sodium	733	733	733	733	733	733	733	733	733	733
Maize starch	206	204	214	112	117	109	89	69	79	—
Pregelat inized maize starch	36	32	20	20	10	—	—	—	—	—
Micro- crystalline	—	—	—	212	110	115	110	130	150	140
Sodium starch glycolate	12	16	20	20	20	20	20	20	20	20
PVP K-30	5	7	8	7	7	7	20	20	20	20
Stearic acid	8	8	8	8	8	8	8	8	8	8

VI. APPLICATIONS

- Provides relief from mild to moderate pain such as headache, muscle ache,toothache and menstrual cramps [11].
- Use for acute treatment for migraine attacks [14].
- Effective in treating soft issue injuries and musculoskeletal pai] [2].
- Used as a part of multimodal analgesia to manage postoperative pain [9].
- Reduces pain and inflammation during acute gout episode [18].

VII. CONCLUSION

The thorough examination of naproxen demonstrates its efficacy as a nonsteroidal anti-inflammatory drug (NSAID) for the treatment of fever, inflammation, and pain. It works by blocking the cyclooxygenase (COX) enzymes, which are essential for the inflammatory process's production of prostaglandins. Patients can benefit from less frequent dosing due to the drug's comparatively long half-life. It must be carefully managed, though, particularly in people who already have medical issues or are taking other drugs that could interact with naproxen.

In every trial, the Naproxen Sodium assay stays within the bounds and conforms to the requirements. The drug release profile in vitro of In purified water, formulation F10 was discovered to be 60 minutes, or 103.5%, is faster than the reference item. The three-month stability study reveals that At 40, the formulation is sufficiently stable. 75% RH and 0°C. It is the flow property of enhance the study of naproxen sodium tablet. Thus, it can be said that the sodium Naproxen the USP 220mg tablet formulation is stable and strong.

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