International Journal of Recent Advances in Multidisciplinary Topics
Volume 3, Issue 3, March 2022
https://www.ijramt.com | ISSN (Online): 2582-7839

Review on Effect of Binders on Nimesulide Tablets

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***Abstract*: Binders are used in tablet formulations to enhance flexibility and hence increase inter particulate bonding strength. The research and development of new excipients are used as binding agents in tablet formulation. This is due to the fact that different binding agents can be used to achieve varying tablet mechanical strengths and drug release qualities for distinct medicinal purposes. Binders are substances that help the granules stick together. The creation of granules of derived hardness and size guarantees the tablet remains intact following compression while also increasing the flow characteristics. The aim of the review is to focus on the effect of the binders like starch, sucrose, tracaganth; hydroxy propyl methyl cellulose, carboxy methyl cellulose, and gelatin possess binding capacity in Nimesulide tablets.**

***Keywords*: Binders, nimesulide, NSAIDs**

1. Introduction

Many modern dosage forms are complex systems including many different components in addition to the active pharmaceutical ingredient (API). These compounds are typically added in addition to the API to protect, sustain, or enhance the formulation's stability. The excipients are chosen based on their concentrations and interactions. Interaction has a direct impact on the drug product's biological, chemical, and physical properties.

A medical formulation development project's goal is to deliver the needed amount of medicine to the patient at the required rate, consistently within a batch, from batch to batch and throughout the product's shelf life [1, 2]. The sulfonanilide compound nimesulide has been shown to be a non-steroidal anti-inflammatory medication (NSAID) with anti-inflammatory, analgesic, and antipyretic properties, as well as a fast onset of action. Since the early 1970's, it has been known that nonsteroidal anti-inflammatory drugs (NSAIDs) have the ability to suppress the synthesis of prostanoids by inhibiting the enzyme cyclooxygenase (COX) 3.

2. Binders

These are dry powders or liquids that are applied to wet granulation to increase granules or cohesive compactness during direct compression. It gives the tablet mechanical strength. Binders come in both powder and liquid form. Powder binders include cellulose, methyl cellulose, polyvinyl pyrrolidine, and PEG. Gelatin, PVP, HPMC, PEG, sucrose, and starch are some of the solution binders. Binders can be added to the formulation in the following ways: as powder before wet agglomeration to ensure uniform distribution of the binder. In wet granulation, it is utilized as an agglomeration liquid in solution form. It's known as a liquid binder [4- 6].

Before compaction, as a dry powder that is blended with other substances (slugging or tableting). It's known as a dry binder. For wet granulation, natural binders such as acacia and tragacanth are employed in solution at a concentration of 10-25 percent, alone (or) in combination, and they can also be added as powder for the direct compression process. When gelatin is combined with acacia (or) used alone, it creates a superior binding agent than the two natural polymers mentioned above. Polymers like as MC and HPMC are employed as dry powders in direct compaction and serve as good binding agents and adhesives in solution form. In alcoholic solutions, ethyl cellulose and HPMC can be utilized as anhydrous adhesives [7].

3. Classification of Binders

1) *Classification on the basis of their source*
   1. Natural polymers: Starch, pre gelatinized starch, gelatin, acacia, tragacanth and gums.
   2. Synthetic polymer: PVC, HPMC, methyl cellulose, ethyl cellulose, PEG.
   3. Sugar: glucose, sucrose, sorbitol.
2) *Classification on the basis of their application*
   1. *Solution binders*: These are dissolved in a solvent (for example water or alcohol can be used in wet granulation processes). Examples include gelatin, cellulose, cellulose derivatives, polyvinyl pyrrolidone, starch, sucrose and polyethylene glycol.
   2. *Dry binders*: These are added to the powder blend, either after a wet granulation step, or as part of a direct powder compression (DC) formula. Examples include cellulose, methyl cellulose [7].

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B. Binders used in nimesulide

1) Starch

Starch is predominantly employed as an excipient in oral solid-dosage formulations, where it acts as a binder, diluent, and dissolver. Freshly made starch paste is employed as a binder in tablet formulations at a concentration of 5-25 percent w/w in tablet granulations. Corn and potato starch that has been well-dried and powdered are the most popular disintegrators. Although starch has a strong affinity for water and swells when wet, allowing the tablets to rupture more easily, other researchers believe that its disintegrating activity is due to capillary action rather than swelling. The starch grains spherical form boosts the tablet's porosity, which promotes capillary action. Although 2% starch is recommended, if faster disintegration is needed, this amount can be increased [8].

2) Sucrose

Sucrose is a sugar made from cane sugar. It hasn't been tampered with in any way. Sucrose is found as colourless crystals, crystalline mass or blocks, sucrose syrup (50-67 percent w/w sucrose), which is used in tableting as a binding agent for well granulations in the powdered form of sucrose. Sucrose is also used as a dry binder (2 percent w/w) or as a bulking agent [9].

3) Tracaganth

Tracaganth gum is available in powdered form as flattened lamellae frequently curved fragments or straights or spiracles twisted linear pieces from 0.52.5mm in thickness. The emulsifying and suspending agent tracaganth gum is utilised. Tracaganth gum is also utilised in cosmetics and food products in a similar way. And it's been employed in tablet formulations as a diluent10.

4) Hydroxy propyl methyl cellulose

After drying, the white or yellowish white fibrous (or) granular powder is almost insoluble in hot water, acetone, ethanol, ether, and toluene, and is almost odourless. It is utilised in the pharmaceutical industry (Tablets excipient and suspending agent).

5) Carboxy Methyl cellulose

CMC is most commonly employed in tablet formulation as a binder, diluent, and disintegrant. Despite the fact that carboxymethyl cellulose is water insoluble. It is an effective tablet disintegrates because it swells 10 times its original mass on contact with water quantities up to 15% w/w may be used in tablet formulations; however, tablets hardness is diminished above this concentration9.

6) Gelatin

Gelatin is a natural protein that works well as a binding agent. It forms tablets that are harder to produce and handle than Hydroxypropyl Methylcellulose. To avoid gelling, warm gelatin solutions must be used. Alcoholic gelatin solutions have been tried, but with little success. According to Tacob and plain11 and sakr12, increasing the gulabin concentration of tablets causes hardness disintegration and dissolves time to increase.

7) Nimesulide Structure

The tolerance and efficacy of nimesulide were compared in a randomised, double-blind parallel group research. (100 mg tds) for one month plus diclofenac (50 mg tds). Throughout the research, all efficacy indicators improved significantly, with no discernible treatment differences. In activated human neutrophils, nimesulide suppresses platelet activating factor production. In the treatment of elderly hyperpyrexia, nimesulide is just as effective and safe as nimesulide [13, 14].

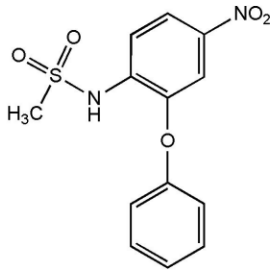

Fig. 1. Nimesulide Structure

Table 1

Mol. Wt	**308.31**
Chemical Name	N-(4-Nitro-2-Phenoxy phenyl) methane sulfonamide.
Category	Non-steroidal anti-inflammatory agent.
Description	Light yellow powder, odourless.
Solubility	Soluble in IN sodium hydroxide, methanol, Chloroform and methylene chloride.
Melting Range	147-151°C

4. Mechanism of Nimesulide

More recently, it has been discovered that there are two COX isoforms: constitutively expressed COX-1, which is linked to physiological prostanoids production, and inducible COX-2, which is linked to prostanoids production at inflammatory locations [15]. In vitro [16, 17] and ex vivo18,19 studies have shown that nimesulide inhibits human cyclooxygenase-2 (COX-2) 5-20 times more effectively than cyclooxygenase-1 (COX - 1). In addition to its impact on the synthesis of prostanoids, nimesulide may have a number of other anti-inflammatory properties. The neutrophil oxidative response is inhibited, cartilage-degrading enzyme synthesis is reduced, histamine action and release are reduced, hyperalgesia mediated by tumour necrosis factor is inhibited, and the release of urokinase, interleukin -620, and elastase is reduced [21].

Even though the elderly is frequently treated with numerous drugs at the same time, and even in patients who have had severe reactions to aspirin or other NSAIDs, this relative safety and tolerability happens in patients of all ages [22].

5. Pharmacokinetics

After oral administration, nimesulide is promptly and virtually fully absorbed. Healthy volunteers received single oral doses of 50 to 200 mg, with mean peak plasma concentrations (c max) ranging from 1.98 to 9.85 mg/L in 1.67 to 3.17 hours (tmax). Food may limit the maximum absorption rate and extent, but not the rate and extent of absorption. Nimesulide has a strong affinity for plasma proteins (99 percent). The extracellular fluid compartment is where nimesulide is mostly found. It enters the synovial fluid, reaching amounts of 44 percent of plasma 3 hours after the injection and 54 percent after 12 hours. Nimesulide appears to spend more time in the

synovial fluid than in the plasma.

1) Indications

In children, nimesulide has been proven to reduce fever and other signs and symptoms of respiratory tract inflammation substantially faster. In children, nimesulide was just as effective at relieving postoperative and musculoskeletal pain as dipyrone, ketoprofen, or paracetamol.

2) Dosage

Adults are usually given 100 mg twice daily of nimesulide. The medicine was given to youngsters in two or three divided doses at a dose of 5 mg/kg/day.

6. Clinical Pharmacology of Nimesulide

Nimesulide is a sulfonanilide non-steroidal anti-inflammatory drug (NSAID) used to treat a variety of inflammatory conditions. It is chemically unrelated to other acid NSAIDs such acetyl salicylic acid and indomethacin. It prevents the release of mediators from human basophils and most other cells. In situations with bacterial Prostatoresiculilis, nimesulide is utilized. Nimesulide has been reported to be an efficient anti-inflammatory medicine with good fenital apparatus diffusion and little negative effects. After a single oral dose of 100 mg of Nimesulide was given to females, the concentration in the genital tissues (uterus, oviduct, and ovaries) was maximum 3 hours later and uniformly distributed throughout the tissues tested [23, 24].

7. Conclusion

Starch, Sucrose, Tracaganth, Carboxy methyl cellulose, Hydroxy propyl methyl cellulose, and Gelatin were chosen as binders because they produced good tablets without any production issues.As a binding agent starches, mucilages, gums can be utilised. They have demonstrated to have strong binding potential as well as other properties such as disintegration agents, fillers, and sustain releasing agents. They have good binding properties in wet granulation, and their granules are more stable and less friable than other binders. They can also be employed to manipulate drug release, affecting absorption and subsequent bioavailability of the integrated medication.

Form this study it is concluded that in tablets formulation binders play a major role which decides the pharmaceutical factors of the tablets and release of drug form the formulation and in turn bioavailability and therapeutic response of the drug.

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