

# FORMULATION AND EVALUATION OF ASPIRIN TABLETS WITH DIFFERENT LUBRICANTS FOR ENHANCED RELEASE KINETICS

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**Abstract:** Aspirin is an NSAID with analgesic, antipyretic, anti-inflammatory, and antiplatelet properties at conventional doses. Lubricants in combination lead to improved medication release kinetics. Lubricants reduce friction by creating a thin fluid layer between tablets and die surfaces, or forming a boundary layer on formulation particles or die surfaces. The prepared tablet is assessed according to bulk density, tapped density, angle of repose, Carr's Index, hardness test, weight variation test, friability test, and in vitro studies. The optimized batch achieved satisfactory results with improved drug release kinetics, following Zero Order Kinetics with the addition of lubricants for enhanced kinetic drug release. The current research intends to produce aspirin tablets using the wet granulation process. In addition to aspirin, the tablets contain HPMC, PVP, Magnesium Stearate, and Talc. The blend is placed into a punching machine, tablets are inspected for weight, diameter, fracture thickness, hardness, break, and dosage, and the findings are assessed. The goal of this study was to examine the lubricants affect over powder flowability, which is crucial in the tablet press.

**Keywords:** Aspirin, lubricants, efficacy, official tests, unofficial tests etc.

## Introduction

Pharmaceutical tablets are made in a number of sequential steps that culminate in compress with a desired shape using a tablet press. Lubricants are added to the powder mixture before tableting phase to guarantee appropriate ejection from the press. The inclusion of lubricants modifies tablet characteristics as well as the behaviour of powder mixture(1). Aspirin, an irreversible NSAID, inhibits cyclooxygenase-1 (COX-1) enzymes, preventing platelet aggregation and modifying the enzymatic activity of thromboxane A2 on platelets. Further thromboxane used to prevent heart attacks, as it binds platelet molecules to form a patch over blood vessel damaged walls, producing long-term effect(2). Aspirin plasma levels range from 3-10 mg/dl for therapeutic doses and 70-140 mg/dl for acute toxicity(3). The present research goal is to produce aspirin tablets using the wet granulation process and further intends to study different lubricants effect over release profile of aspirin tablets. Lubricants are commonly used to aid in the tableting of many formulations. After compression, a tablet must be ejected from the tablet press die. Lubricants reduce friction between the tablet and the die's metal surface, lowering the ejection force

and ensuring that the tablet is ejected precisely and without cracking or breaking. Lubricants reduce friction by creating a thin fluid layer between tablets and die surfaces, or forming a boundary layer on formulation particles or die surfaces(1). Common boundary lubricants include metallic fatty acid salts, fatty acids, esters, sulfates, polymers, and inorganic materials. Magnesium stearate, a cost-effective, high-performance, and chemically stable lubricant, is a popular choice for pharmaceutical tableting due to its high melting point(4). Stearic acid is a popular fatty acid boundary lubricant, used at 2.5 wt.%, while talc is an inorganic lubricant used when other lubricants are insufficient due to chemical instability, adding 1.0 to 10.0 wt.%(4).

Lubricants are essential for tableting tablets, but can alter their properties in unwanted ways. Magnesium stearate, a common lubricant, can negatively impact the hardness of tablets made from malleable materials. Combining it with microcrystalline cellulose can decrease tablet strength. Other lubricants also have negative effects. Because many lubricants are hydrophobic, adding lubricant can reduce tablet disintegration and dissolving rates. Multiple investigations have

indicated that the detrimental effects are a result of the lubricant's huge surface area and hydrophobicity.

Many methods have been devised to assess the flow characteristics of granules. These procedures generally involve static Angle of repose, Carr's compressibility index, Hausner ratio, and shear cell testing(5). Powder flow is crucial for tableting, affecting weight uniformity and consistent quality. Physical factors like particle size, density, surface morphology, and shape influence powder flow. Smaller particles with low densities and uneven surfaces flow slower than larger, smooth, and spherical ones. Particle shape and surface morphology affect friction, affecting powder flow(6).

In addition to aspirin, the tablet contains hydroxypropyl methylcellulose (HPMC), polyvinylpyrrolidone (PVP), magnesium stearate, and talc. The blend is placed into a punching machine, tablets are inspected for weight, diameter, fracture thickness, hardness, break, and dosage, and the findings are assessed(7). The particles to be compressed are made up of one or more medicaments, with or without excipients such as diluents, binders, and disintegration agents, as well as lubricants, glidants, and chemicals that may alter the formulation behaviour in the digestive tract. Such chemicals must be harmless and therapeutically inert in the quantities present.

Conventional oral dosage forms can cause fluctuations in drug plasma levels, depending on the agent's half-life, frequency of administration, and release rate(8). This study uses aspirin as a model medicine due to its analgesic and antipyretic properties. They are meant for oral administration. Some tablets are taken whole or after chewing, while others are dissolved or dispersed in water before delivery, and some are held in the mouth, releasing the active component. Tablets may be used for administration via implants and passerines, but may require special formulations or presentation forms. Tablets have various properties based on composition, manufacturing method, or

application. Unless specified, tablets are uncoated, and coating is permitted if specified. Where coating is permitted, the monograph directs coating, and the sentence reads "The tablets are coated". Unless otherwise specified, tablets can be coated in one of several ways(9).

Tablets are the most common unit solid dose form for oral drugs, used for systemic effects and over 90% of marketed pharmaceuticals due to advantages like ease of handling, stability, and self-medication possibilities. There are several types of tablets on the market, with uncoated and coated tablets falling into one category(10). Some medications may get destroyed in the gastrointestinal environment, while others may irritate the mucosa. NSAIDs, as well as powerful antibiotics such as erythromycin and azithromycin, can have this effect. Layers of coating solution are put to these pharmaceuticals to produce a thick cover around the tablet, which may keep the drug from being exposed to acidic environments and, more importantly, preventing gastrointestinal discomfort and irritation.

**Lubricants:** Lubricants prevent material clumping and stickiness in tablet punches or capsule filling machines, ensuring minimal resistance between solid and die walls. These are used to improve the overall processing properties in tablets or firm gelatine capsules.

**Table no. 1:** Lubricants Used in Tablet Formulation(4).

| S. No. | Lubricants | Examples                                    |
|--------|------------|---------------------------------------------|
| 1      | Minerals   | talc or silica,                             |
| 2      | fats       | stearin, magnesium stearate or stearic acid |

**Binders:** Binders are essential components in tablets, ensuring mechanical strength and volume for low active dosage tablets, and are typically used to hold ingredients together.

**Table no. 2:** Lists of various binders used during granules formation for the preparation of tablets(11).

| S. No. | Different Binders Classes | Examples                                                                        |
|--------|---------------------------|---------------------------------------------------------------------------------|
| 1      | Saccharides               | Sucrose, lactose                                                                |
| 2      | Polysaccharides           | Starches, cellulose as micro crystalline cellulose hydroxypropyl cellulose      |
| 3      | Sugar alcohols            | Xylitol, sorbitol or maltitol                                                   |
| 3      | Protein:                  | gelatin                                                                         |
| 5      | Synthetic polymers        | PVP, polyethylene glycol (PEG).                                                 |
| 6      | Solution binders          | Polyvinylpyrrolidone, starch, sucrose and polyethylene glycol, water or alcohol |
| 7      | Dry binders               | Methylcellulose, PVP, and Polyethylene glycol.                                  |

## Materials and Methods

**1. Materials:** Aspirin from Saphnix Lifesciences, India, HPMC from Triveni, India, PVP from Pushkar Pharma, India, sodium stearate from Metlub Enterprises, India, and talc from Vasundhara Micro Mineral Infinite Pvt. Ltd., India etc. All chemicals and reagents were of analytical quality.

**Instruments:** UV- visible spectrophotometer (Shimadzu, Japan), Single sided Rotary Tablet Punching Machine (Proton Tablet Press, India), Analytical Balance of readability 0.0001g (Infitek, India), Vernier Caliper (Baker, India), Disintegration Testing Apparatus (Erweka, Japan) etc.

The initial phase involved preparing and testing granule compositions (refer table no. 3).

**Table no. 3.** The composition of granules (amounts of the substances are given in parts).

| Granules | Aspirin | HPMC | Microcrystalline Cellulose | PVP | Magnesium Stearate |
|----------|---------|------|----------------------------|-----|--------------------|
| F1       | 250     | 50   | 70                         | q.s | 1                  |

|    |     |    |    |     |     |
|----|-----|----|----|-----|-----|
| F2 | 250 | 50 | 70 | q.s | 1.5 |
|----|-----|----|----|-----|-----|

## 2. Calibration Curve Preparation

A calibration curve is a graph that shows the correlation between a substance's concentration and its detected output. The curve is used to calculate the concentration of an unknown drug(12). The  $\lambda_{\max}$  of aspirin from literature review was concluded at 254nm and same was considered for further preparation of analytical curve(13). During experimentation we have prepared various concentrations of aspirin that were, 0.5 $\mu$ g/ml, 1  $\mu$ g/ml, 1.5  $\mu$ g/ml, 2  $\mu$ g/ml, and 2.5  $\mu$ g/ml by using phosphate buffer as vehicle (refer to table no. 4). Further calibration curve was constructed by analysing different solutions by UV spectrophotometer apparatus and obtained a straight line with Regression coefficient of 0.9965.

**Table no.4:** Calibration curve of aspirin.

| S. no. | Concentration X- axis ( $\mu$ g/ml) | Absorbance Y- axis (nm) |
|--------|-------------------------------------|-------------------------|
| 1.     | 0                                   | 0                       |
| 2.     | 0.5                                 | 0.125                   |
| 3.     | 1                                   | 0.243                   |
| 4.     | 1.5                                 | 0.332                   |
| 5.     | 2                                   | 0.435                   |
| 6.     | 2.5                                 | 0.543                   |

## 3. Preparation of Phosphate buffer(pH7.2):

Prepare 800ml of distilled water and accurately weigh 20.214 g Sodium Phosphate Dibasic Heptahydrate. Add Sodium Phosphate Dibasic Heptahydrate (20.214 g) in above prepared distilled water. Now, add 3.394 g sodium phosphate monobasic monohydrate to the above solution. Add distilled water until the solution volume reaches 1 l. Finally check the pH of buffer by using pH meter(13).

## 4. Preparation method of tablets(14):

To study lubricant effects, two distinct batches of the tablet were made by utilizing the wet granulation process. The composition of a tablet of each batch is shown in Table no. 5.

- The amount that was determined required for manufacturing 400 mg aspirin tablets containing 250 mg of pure aspirin, HPMC polymer, and PVP as a binder was uniformly mixed.
- To prepare the wet bulk, an adequate amount of granulating solution (purified water) was gently supplied to above prepared uniform mixture. Further granules were produced by sieving the wet mass through a 20 no. sieve.
- The desired quantities of granules were weighed and compacted using an automatically operated tablet punching machine with a 12mm flat faced punch diameter. Lubricants (Magnesium stearate and talc) in granules have been used during tablet preparation to maintain the low resistance between the granules and the die wall.
- The compressed tablet batches were stored in sealed containers at room temperature for future research.

**Table no. 5:** Formula indicating the composition of tablets batches.

| S. no. | Ingredients (mg)           | F1    | F2   |
|--------|----------------------------|-------|------|
| 1      | Aspirin                    | 250   | 250  |
| 2      | HPMC                       | 50    | 50   |
| 3      | Microcrystalline cellulose | 70    | 70   |
| 4      | PVP                        | Q. S. | Q.S. |
| 5      | Talc                       | 5     | 10   |
| 6.     | Magnesium Stearate         | 1     | 0.5  |

## Evaluation of aspirin tablets

### 1. Granules evaluation parameters:

- Angle of Repose(15): The angle of repose of the granule blend was determined using the fixed funnel method. A funnel was used to collect the correctly weighed quantity of granules. The funnel's height was adjusted such that the tip just touched the apex of the mound of granules. Granules are allowed to flow freely through the funnel onto the surface. The powder cone's diameter was measured, and angle of repose was determined using the following equation.  
 $\tan \Theta = h/r$ ,  $\Theta = \tan^{-1}(h/r)$
- Where  $\Theta$  is the angle of repose,  $h$  is the cone's height in cm, and  $r$  is the base radius in cm.
- Bulk density ( $B_p$ )(16): Bulk density was calculated by pouring the granules into a graduated cylinder in a bulk density instrument. The bulk volume ( $V_b$ ) and mass ( $m$ ) of the granules were measured. The bulk density was computed using the following formula.  

$$B_p = m/V_b$$
- Tapped density ( $T_p$ ): In the bulk density apparatus, a measuring cylinder containing a known mass ( $m$ ) of granule blend was tapped 1000 times for a set time. The lowest volume filled by the cylinder ( $V_t$ ) and mass of the granules ( $m$ ) was determined. The tapped density was determined using the following formula.  

$$T_p = m/V_t$$
- The compressibility index (Carr's Index): The compressibility index defines the flow characteristics of Carr's granules. The % compressibility of granules is a direct indicator of possible powder morphology and consistency. The Carr's index can be determined using the following formula.  

$$\text{Carr's Index} = \frac{T_p - B_p}{B_p} * 100$$
- Where  $T_p$  is the tapped density of granules and  $B_p$  is the bulk density of the granule.
- Hausner's ratio: It is used to determine the flow properties of granules. It is derived by dividing the tapped density by the bulk density. The equation is

$$\text{Hausner's ratio} = \frac{T_p}{B_p}$$

The values obtained from above calculations shows the flow characteristics of prepared granules. The values are cross checked with Table no. 6 flowability scale of granules.

**Table no. 6:** Flowability scale as assessed by several approaches.

| S. No. | Flow property  | Angle of repose | Compressibility index | Hausner's ratio |
|--------|----------------|-----------------|-----------------------|-----------------|
| 1.     | Excellent      | 25-30           | 10                    | 1.00-1.11       |
| 2.     | Good           | 31-35           | 11-15                 | 1.12-1.18       |
| 3.     | Fair           | 36-40           | 16-20                 | 1.19-1.25       |
| 4.     | Passable       | 41-45           | 21-25                 | 1.26-1.34       |
| 5.     | Poor           | 46-55           | 26-31                 | 1.35-1.45       |
| 6.     | Very poor      | 56-65           | 32-37                 | 1.46-1.59       |
| 83     | Very very poor | -               | -                     | 1.6             |

## 2. Post compression parameters for aspirin tablets(17)(18):

- **Weight Variation Analysis:** The weight variation of tablets was examined using a digital analytical balance in accordance with the USP XXIV monograph. Twenty tablets from each batch were used to determine weight variance between tablets, and the mean and standard deviation were determined.
- **Friability testing:** The friability of a tablet can be determined in the laboratory using the Roche Friabilator. This comprises of a plastic transparent cylinder that rotates at 25 rpm. Tablets were used to test friability in accordance with the USP XXIV monograph. Friability testing was done by Roche Friabilator, with readings in triplicate. The percentage of friability was estimated using the equation below.

$$\text{Friability (\%)} = \left(1 - \frac{WF}{WI}\right) * 100$$

Where WI and WF represent the weights of the tablets before (initial weight) and after (final weight) the test, respectively.

- **Hardness analysis:** Tablets require a specific level of strength or hardness, as well as resistance to friability, to survive mechanical vibrations during manufacturing, packaging, and transportation. Hardness is a measure of the tablet's crushing strength. The hardness of the tablets was measured using a Pfizer hardness tester.
- **Thickness:** The thickness of the sustained release tablets was measured using a Vernier calliper. The data were expressed as the mean values of 10 tests, with standard deviations.
- **Disintegration Testing:** The U.S.P. disintegration testing apparatus consists of six 3-inch-long glass tubes with an open top and ten mesh screens at the bottom end. During the disintegration test, one tablet is placed in each tube and the basket rack is positioned in a 1 l beaker of distilled water at  $37 \pm 2^\circ\text{C}$  such that the tablet remains 2.5 cm below the surface of the liquid on upward movement and not closer than 2.5 cm from the bottom of the beaker on downward movement. Move the basket with the tablets up and down 5-6 cm at a rate of 28 to 32 cycles per minute.
- **Drug Content:** The tablets were crushed, and 250 mg equivalent weight of aspirin in tablet powder was precisely weighed and transferred to a 100 ml volumetric flask. Initially, 10 ml of phosphate buffer (pH 7.2) was added and mixed for 10 minutes. Following that, buffer was added to increase the capacity to 100 ml. The solution in the volumetric flask was then filtered, and 1 ml of the filtrate was diluted and measured at 265 nm using a UV-visible spectrophotometer (Shimadzu UV-1800, Japan). The drug content of each sample was

estimated using the previously generated standard curve.

- **Dissolution test:** The dissolution of commercially available brands and manufactured aspirin tablets was determined using the paddle method in a dissolution equipment with phosphate buffer solution 500 mL (pH 7.2) at 50 rpm and  $37 \pm 0.5^\circ\text{C}$ . After 30 minutes, the absorbance of suitably diluted portions in the same medium was compared to the absorbance of a standard preparation at 265nm using a UV-VIS Spectrophotometer (Shimadzu UV-150-02 Double beam spectrophotometer).
- **Drug Release Kinetics:** The kinetics of drug release was examined in 900 ml of phosphate buffer (pH 7.2) at  $37 \pm 2^\circ\text{C}$  and 100 rpm for six hours. After a given time interval, 5ml of the sample was taken and replaced with an equal volume of fresh dissolving media. Twenty collected samples were evaluated spectrophotometrically at a measured wavelength of 265 nm, and the cumulative percent drug release was measured.

## Results and Discussion

### 1. Pre-compression parameters of aspirin tablets:

Angle of repose, bulk density, tapped density, Carr's index, and Hausner's ratio were all measured for all batches. It is seen that all parameters fall inside the defined range. It is given in Table no. 7.

**Table no. 7:** Flowability parameters of aspirin granules.

| S. no. | Formulation code | Angle of repose (degree) $\pm$ S.D | Bulk density (g/ml) $\pm$ S.D | Tapped density (g/ml) $\pm$ S.D | Carr's Index (%) $\pm$ S.D | Hausner's Ratio $\pm$ S.D |
|--------|------------------|------------------------------------|-------------------------------|---------------------------------|----------------------------|---------------------------|
| 1.     | F1               | $25.10 \pm 0.11$                   | $0.489 \pm 0.04$              | $0.577 \pm 0.15$                | $8.55 \pm 0.06$            | $1.08 \pm 0.15$           |

|    |    |                  |                  |                  |                 |                 |
|----|----|------------------|------------------|------------------|-----------------|-----------------|
| 2. | F2 | $24.98 \pm 0.10$ | $0.487 \pm 0.16$ | $0.610 \pm 0.10$ | $6.87 \pm 0.08$ | $1.09 \pm 0.16$ |
|----|----|------------------|------------------|------------------|-----------------|-----------------|

Note: All values are expressed as mean  $\pm$  S.D, with a sample size of three.

### 2. Post-compression parameters of aspirin formulations:

All post-compression parameters of prepared batches are tested accordingly, including thickness, hardness, friability, weight fluctuation, medication content, and tablet diameter. It is seen that all parameters fall inside the set limit. The batches results are mentioned in Table 8.

**Table no.8:** Post-compression parameters of aspirin tablets (Unofficial tests)

| S. no. | Parameters                      | Batch F1         | Batch F2         |
|--------|---------------------------------|------------------|------------------|
| 1.     | Diameter (cm) $\pm$ S.D n=10    | $8.19 \pm 0.06$  | $8.02 \pm 0.03$  |
| 2.     | Hardness (kg) $\pm$ S.D n=10    | $8.8 \pm 0.023$  | $8.7 \pm 0.022$  |
| 3.     | Thickness (mm) $\pm$ S.D n=10   | $2.76 \pm 0.011$ | $2.75 \pm 0.012$ |
| 4.     | Friability(w/w%) $\pm$ S.D n=20 | $0.26 \pm 0.12$  | $0.30 \pm 0.18$  |

**Table no. 9:** Postcompression parameters of aspirin tablets (Official tests)

| S. no. | Parameters                              | Batch F1            | Batch F2            |
|--------|-----------------------------------------|---------------------|---------------------|
| 1.     | Weight variation (mg) $\pm$ S.D n=20    | $0.072 (\pm 0.025)$ | $0.074 (\pm 0.022)$ |
| 2.     | Disintegration Time (min) $\pm$ S.D n=6 | $32 \pm 2$          | $37 \pm 1$          |
| 3.     | Average dissolution (%) n=6             | 88.23               | 85.01               |
| 4.     | Drug content (mg) $\pm$ S.D n=20        | $248.0 \pm 0.12$    | $249.0 \pm 0.19$    |

## Conclusion:

During present study, the two batches of aspirin tablets were prepared using the wet granulation method. Aspirin tablets with fewer excipients were successfully made and met all pharmacopoeial restrictions. After conduction of all evaluation parameter, it was concluded that F1 formulation has shown greater efficiency.

This type of research might potentially be conducted on other pharmaceuticals to develop a cost-effective product. Future studies should use the current data as a reference guide to do additional research using the optimization technique.

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