IJARSCT
ISSN (Online) 2581-9429
International Journal of Advanced Research in Science, Communication and Technology (IJARSCT)
Volume 2, Issue 2, December 2022
Impact Factor: 6.252

Review on Preparation and Evaluation of 300 mg Aspirin Tablet by Wet Granulation Method

Tambe Aditya[1], Tarade Akshay[2], Waghamare Rahul[3], Dapkekar Sambhaji[4], Prof. Datkhile Sachin[5]
Students, Samarth Institute of Pharmacy, Belhe, Maharashtra,India[1, 2]
Department of Pharmaceutics, Samarth Institute of Pharmacy, Belhe, Maharashtra, India[1, 2, 3]
akshay.tarade2001@gmail.com

Abstract: The goal of the current study was to create aspirin tablets using the wet granulation method with less excipients and to evaluate how it performed against other brands. In addition to aspirin, the design formulation also included excipients such lactose, maize starch, and aerosil. The mixture was compressed using a single punch machine, and the tablets were then put through a series of tests (including ones for uniformity of weights, diameter and thickness, hardness, disintegration, dissolution, and drug assay), with the results being compared to those of some of the competing brands. The investigated formulation closely resembled the commercially available brands and complied with all official requirements. To create a solution that is affordable, additional research should be planned utilizing different active ingredients and excipients.[1]

Keywords: Aspirin, Acetyl salicylic acid, direct compression, Dissolution, Disintegration, Hardness. [2]

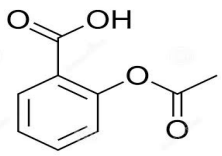
I. INTRODUCTION

Though, pharmaceutical research have been focused on development of new and more compliant dosage forms, tablets still remain popular due to their stability, ease of handling and convenience of dosing and account for more than 80% of all dosage forms administered (Jivraj et al., 2000). [13] These are manufactured by wet granulation, dry granulation and direct compression (DC) methods (Jones, 2008). DC is advantageous over other methods of tablet manufacturing as it requires fewer unit operations, consequently low cost and less time consumption, generates optimum possible bioavailability (Yasmeen et al., 2005), low microbial level due to absence of moisture (Ibrahim and Olurinola, 1991) and produces faster dissolution rates for certain compounds (Jivraj et al., 2000). This method is preferred for tablet manufacturing especially in case of thermolabile and moisture-sensitive drugs (Jivraj et al., 2000).[3] Aspirin is a commercial example of a DC tablet granulation prepared by the dry granulation technique. It is most widely used drug in the world (Michael Gossop, 2007) as an analgesic, anti-inflammatory and antipyretic agent (Sweetman, 2009), however, many workers have investigated its clinical profiles in a number of other medical conditions such as cardiovascular (Buring, 2006, Moyad, 2001, Berger et al., 2009), cancer (Moyad, 2001, Chan et al., 2009, Cook et al., 2005) and diabetes (Yang et al., 2009, Ong et al., 2010) and have found promising results. The objective of the present study was to make a new formulation of aspirin tablets by DC using a fewer excipients in three trail batches and to compare this formulation with the available brands in the local market containing aspirin in the same strength. [4]

1.1 Types of Tablets

1. On the basis of drug release tablets

(a) Mediated release tablets



Aspirin
Acetylsalicylic acid

$C_9H_8O_4$

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(b) Modified release tablets

- Extended release tablets Delayed release tablets

2. On the basis of methods of manufacturing

- Compressed tablets Molded tablets

3. On the basis of route of administration

(a) Oral tablets for ingestion:

1. Compressed tablets
2. Multiple compressed tablets
3. Delayed action tablets
4. Sugar coated tablets
5. Film coated tablets
6. Chewable tablets
7. Targeted tablet
   - Floating tablet
   - Colon targeting tablet
8. Dispersible tablets:

(b) Tablets used in oral cavity.

1. Buccal tablets
2. Sublingual tablets
3. Troches and Lozenges
4. Dental cones

(c) Tablets administered by other routes

1. Implantation tablets (or depot tablets)
2. Vaginal tablets (or vaginal insert)

IV. On the basis of types of dosage form ingested

(a) Tablets used to prepare solution

1.Effervescent tablets

2. Dispensing tablets
3. Hypodermic tablets
4. Tablet triturates

(a) Tablets used as such

(b) Example: Remaining all.

1. **Compressed Tablet:** These tablets are uncoated, made by compression of granules and usually intended to provide rapid disintegration and drug release. These tablets, after swallowing, get disintegrated in the stomach, and its drug contents are absorbed in the gastrointestinal tract and distributed in the whole body.
2. **Multiple Compressed Tablets:** These tablets are prepared to separate incompatible (physically or chemically) ingredients or to produce repeat action/prolonged action products. Repeat action tablet: Repeat-action tablets are a type of extended-release dosage form which contain two single doses of medication, one for immediate release and one for delayed release. Typically, the immediately released drug comes from the exterior portion of the tablet and the delayed release coming from the interior portion. Essentially, there is a tablet within a tablet, with the interior tablet having a coating that delays release of its contents for a predetermined time.
3. **Delayed Release Tablet:** These are the dosage forms which release portions of drug at a time other than promptly after administration. An initial portion may be released promptly after administration. Enteric-coated dosage forms are common delayed-release products. Sugar coated tablet: The tablet that contains active ingredient(s) of unpleasant taste may be covered with sugar to make it more palatable. This type of tablet should be administered in whole form; otherwise the patient will experience the unpleasant taste of the active ingredient.

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4. **Film Coated Tablet:** The tablet that is covered with a thin layer or film of polymeric substance which protects the drug from atmospheric conditions and mask the objectionable taste and the odor of drug.
5. **Buccal Tablet:** "Buccal tablets", which means that instead of being swallowed like a normal tablet, they should be dissolved in the mouth. They should not be swallowed whole or chewed. The tablet is placed high up along your top gum, under the upper lip either side of your mouth. The tablet will soften and stick to the gum, and will dissolve completely after a few hours.
6. **Sublingual Tablet:** The drug which is destroyed or inactivated within the gastrointestinal tract but can be absorbed through the mucosal tissue of the oral cavity is usually given in this formulation. The tablet is required to be placed below the tongue for the slow release of drug. But for immediate effect some medicaments are formulated in such a way to dissolve within 1 to 2 minutes. Nitroglycerin is prepared in this formulation.
7. **Troches or Lozenges:** Lozenges are solid preparations that are intended to dissolve or disintegrate slowly in the mouth. They contain one or more medicaments usually in a flavored, sweetened base. Lozenges are most often used for localized effects in the mouth. They can also be used for systemic effect if the drug is well absorbed through the buccal lining or is swallowed. Lozenges can be made by molding or by compression. The name troche is applied to compressed lozenges.
8. **Dental Cone:** A tablet form intended to be placed in the empty socket following a tooth extraction, for preventing the local multiplication of pathogenic bacteria associated with tooth extractions. Implantation tablets: A small tablet that is prepared for insertion under the skin by giving a small surgical cut into the skin which is stitched after the insertion of the tablet. This tablet must be sterile one. The drug used in this preparation is usually water insoluble and the tablet provides a slow and continuous release of drug over prolonged period of time ranging from 3 to 6 months or even more. Contraceptive tablet is formulated as implant.
9. **Vaginal Tablet/Pessary:** Pessaries are solid medicated preparations designed for insertion into the vagina where they melt or dissolve. Moulded pessaries are cone shaped and prepared in a similar way to Moulded suppositories. Compressed pessaries are made in a variety of shapes and are prepared by compression in a similar manner to oral tablets.
10. **Effervescent Tablets:** The tablet that contains acid substances and carbonate or hydrogen carbonate that react rapidly in the presence of water to release carbon dioxide. Sodium bicarbonate, citric acid and tartaric acid are added to the active ingredients to make the tablet effervescent. This preparation makes the tablet palatable.
11. **Dispensing Tablet:** These tablets are prepared for providing an accurate and convenient quantity of drug that can be incorporated readily in compounding other dosage form. Tablets are solely designed to provide a convenient quantity for administration as a dosage form, because sometimes they contain very potent drugs which may prove fatal.
12. **Hypodermic Tablet:** It is a compressed or molded water-soluble tablet that contains a specified amount of medication and is intended for hypodermic administration, Tablet triturate: These are powders molded into tablets. Molded tablets are flat, circular disc and usually contain a potent substance which is mixed with lactose, dextrose or some other suitable diluent. The apparatus used for the preparation of tablet triturates is made of stainless steel or plastic.

II. PROCEDURE FOR TABLET PREPARATION

There are two Methods by which Dry Granules are formed:

(1) Slugging and (2) Roller Compaction.

(a) Slugging: In this technique, the powders are mixed (as described previously) and then compressed into a primordial oversized tablet using a tableting press that is capable of applying a high stress (to ensure that aggregation of the particles and then aggregation of granules occur during compaction). Following this the tablet is milled to produce granules of the required size.

(b) Roller compaction: In roller compaction, the formulation ingredients are mixed and are then compressed using a roller compactor. In this, the powders are fed from a hopper on to a moving belt and then transported to, and

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compressed by, the passage between the narrow gaps between two (oppositely) rotating rollers to produce a sheet/film of compressed material. The compressed sheet is then milled to produce granules of the required size. [14]

Direct Compression:

Direct compression method is the process by which tablets are compressed directly from powdered active drug substance and suitable excipients into a firm compact without employing the process of granulation.

Procedure:

1. Accurately weighed specified quantity of binders (microcrystalline cellulose and Povidone K30) and active pharmaceutical ingredient (Aspirin) are mixed properly.
2. Add required quantity of disintegrant (sodium starch glycolate) and then add glidant (Purified talc), mix the mixture well.
3. Then lubricate this mixture with required quantity of magnesium stearate and mixed the blend well for 15 minutes by using tumbling method.
4. The powder mix is compressed into tablet by using tablet punching machine. [12]

Sr. no.	Ingredients	Quantity given (1 tablet)	Quantity taken (40 tablet)	Role of ingredients
1.	Aspirin	300mg	12gm	Antipyretic, Analgesic
2.	Citric acid	30mg	1.2gm	Masking agent
3.	Calcium Carbonate	100mg	4gm	Solubilizer
4.	Saccharine sodium	3mg	0.12gm	Sweetner
5.	Starch	10%	Qs	Binder
6.	Sodium EDTA	3mg	0.12gm	Chelating agent
7.	Magnesium stearate	4mg	0.16gm	Lubricant
8.	Starch	30mg	1.2gm	Binder or diluent
9.	Talc	20mg	0.4gm	Glidant

Evaluation of Aspirin Tablets:

Physical Parameters

Color	White
Odor	Odorless
Taste	Bitter

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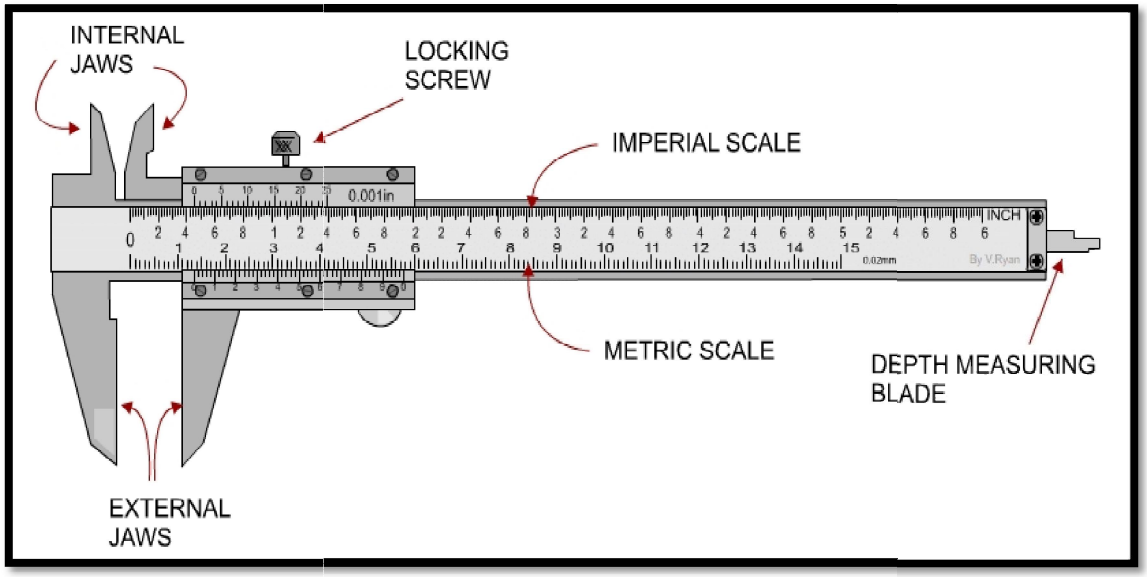
1. Weight variation test of Aspirin Tablets

Weight variation test of each trail formulation and commercial brands was carried out by taking average weight of 20 individually weighed tablets on an analytical balance (Sartorius GmbH type a 6801) and compared with permissible limits.

2. Diameter and Thickness

Random samples of 10 tablets were selected from each of the trial batches and Commercial brands and their diameter and Thickness was calculated in centimeters with the help of micrometer screw gauge or Vernier calliper.



3. Hardness test of Aspirin tablets

Hardness of randomly selected 10 tablets of each brand and trial formulation batch was measured using Hardness Tester (Monsanto Hardness Tester). Load was given to tablets in a diametric direction to determine an actual load when the tablet was broken.

4. Friability Test for Aspirin tablets

Friability test was performed on twenty randomly selected tablets of each brand and Trial formulation batches which were cleared from any loose dust with help of soft brush and weighed accurately for their initial weight. Each set of tablets were placed separately in Friability Tester (H. Jurgens and Co- GmbH, D2800, and Germany) and run for 4 minutes (25rpm). After removing from tester, tablets were cleared from any loose dust and their Final weight was determined to calculate loss of weight which is indicative of mechanical strength to withstand this type of wear.

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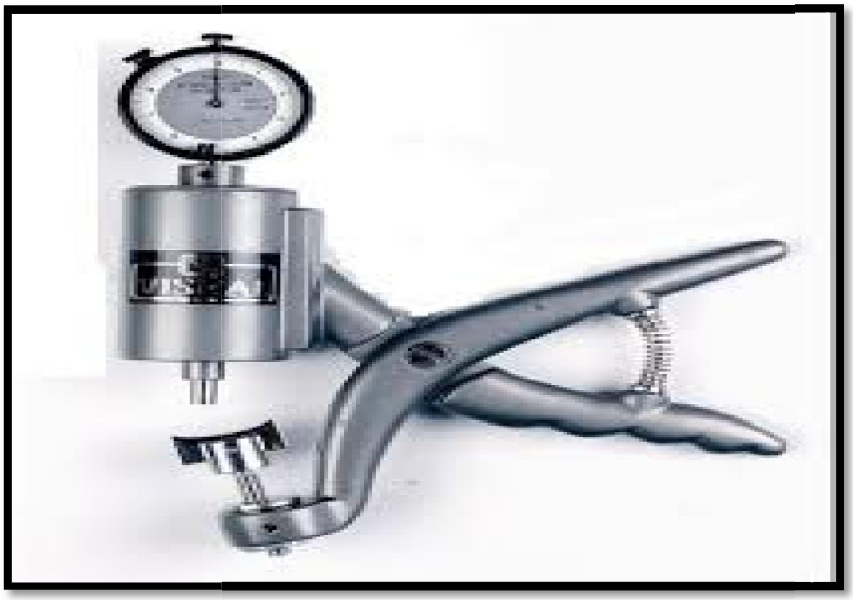

5. Disintegration test for Aspirin Tablets

Disintegration time was measured by putting 6 tablets of each of the studied formulation separately in basket rack assembly (Erweka ZT-2, Germany) using disks to avoid floating of tablets in 900 ml distill water maintained at 37±2ºC.

6. Dissolution Test for Aspirin Tablets

Dissolution of commercially available Brands and formulated aspirin tablets was Measured by paddle method in dissolution Apparatus (Erweka GmbH, Germany) using 0.05M acetate buffer solution 500 mL (pH 4.5) At 50 rpm, maintained at 37±0.5°C. After 30 Minutes the absorbance of suitably diluted Portions in same medium was determined against absorbance of standard preparation at 265nm using UV-VIS Spectrophotometer (Shimadzu UV-150-02 Double beam Spectrophotometer).

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7. Assay of Aspirin tablets

Twenty tablets were accurately weighed and than triturated in a mortar with pestle, amount equivalent to 100 mg of aspirin was transferred to a 50 mL volumetric flask, diluted by 20 mL of diluting solution (acetonitrile and formic acid 99:1). The volumetric flask was shaken manually, centrifuged at 3000 rpm for 5 minutes and than the stock prepared was diluted. An aliquot of the diluted solution was injected into a liquid chromatograph with a detector set at 280 nm. The responses were compared with the standard to determine the quantity in mg of aspirin present in the sample.

III. PHARMACOLOGICAL ACTIVITY

3.1 Analgesic activity

The analgetic effect of ASPIRIN* has been recognized and utilized clinically for more than half a century. The degree of analgesia attained with ASPIRIN* is moderate but it has proved highly suitable in the management of pathological pain of mild to moderate severity. As regards site of action, both peripheral and CNS factors appear to contribute significantly to the pain relief afforded by ASPIRIN*. As for mechanism of action, the accumulated evidence of recent years indicates that ASPIRIN* acts by interfering with the synthesis and release of prostaglandins, thereby averting the sensitization of pain receptors to mechanical stimulation or to other mediators. [5]

3.2 Migraine

Migraines are reoccurring headaches that last 4-72 hours and are characterized by Lateralized throbbing, moderate to severe pain intensity and at least one other of the Following symptoms: nausea, photophobia, phonophobia. Routine physical activity Aggravates the symptoms. Some individuals also experience neurological aura such as blurring of vision before the pain and associated symptoms occur. Evidence suggests that there are at least three mechanisms involved in the pathophysiology of migraines: extracranial arterial vasodilatation, extracranial neurogenic inflammation and decrease inhibition of central pain transmission. It has been shown that the degree of inflammatory activity is proportional to the intensity of the pain felt and as the blood pulses, the characteristic throbbing emerges. An estimated two million Canadians have been diagnosed with migraines but many migraineurs never receive a clinical diagnosis; therefore, the actual numbers of Canadians who suffer from migraines could be over 3 million. Over 70% of migraine suffers are women and the majority are aged between 20 and 50 years. This prevalence is based in part due to hormonal fluctuations that women experience related to menstruation, oral contraceptive use, pregnancy, and menopause and hormone replacement therapy. The use of a single dose of ASPIRIN* (2 x 500mg tablets) in patients with a migraine attack was investigated in two placebo-controlled clinical studies conducted by Bayer. Treatment with ASPIRIN resulted in a statistically significant relief of migraine pain and inthe associated symptoms of photophobia and phonophobia that continued throughout the 6Hour post-dose observation. The results also showed a significant improvement in overall Quality of life for migraine sufferers but there was no difference between ASPIRINandPlacebo groups in headache recurrence. [6]

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3.3 Antipyretic Activity

Interference with the synthesis and release of prostaglandins is also involved in the antipyretic activity of ASPIRIN. ASPIRIN effects a significant reduction in elevated body temperature, but has little effect on normal body temperature. This latter is maintained by a delicate balance between heat production and heat loss, with the hypothalamus regulating the set point at which body temperature is maintained. Fever is induced by synthesis and release of prostaglandins in this temperature-regulating area and ASPIRIN acts by interfering with this process. Heat production is not inhibited but dissipation of heat is augmented by increased peripheral blood flow and by sweating. [7]

3.4 Anti-inflammatory Effect

Components of the anti-inflammatory action of the salicylates are increased capillary resistance, thus reducing capillary leakage in response to local toxins, interference with the production of tissue-destructive lysosomal enzymes and inhibition of the synthesis of

Prostaglandin E compounds which have been shown to be potent mediators of the inflammatory process. Besides interfering with the synthesis of prostaglandins ASPIRINalso acts by interfering with lymphocyte activation and lymphokine production.[8]

Lymphokines are produced by activated thymus lymphocytes which are abundant in the inflammatory tissues of patients suffering from rheumatoid arthritis. They cause increased vascular permeability and white blood cell chemotaxis, activate macrophages and stimulatelymphocyte DNA synthesis. They also induce release of tissue-destructive lysosomalenzymes as well asprostaglandins. The prostaglandins themselves, besides causing many manifestations of inflammation also act as a potent negative feedback mechanism byinhibiting lymphokine production. An in depth review of the effects of ASPIRIN on the lymphocyte-macrophage axis in inflammation has recently been published. [9]

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ISSN (Online) 2581-9429
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