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ASPIRIN: AN OVERVIEW AND DEVELOPMENT OF ITS DOSAGE FORM

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ABSTRACT :

This report provides a comprehensive overview of anti-inflammatory drugs, focusing on the mechanism, classification, and therapeutic uses of non-steroidal agents such as aspirin. It highlights aspirin's pharmacological actions including its analgesic, antipyretic, anti-inflammatory, and antiplatelet effects. The study also details the preformulation studies of aspirin, encompassing physical, chemical, micromeritic properties, and stability profiles essential for effective dosage form development. Furthermore, the document outlines various aspirin tablet formulations, manufacturing methods like wet granulation and direct compression, and evaluation parameters such as weight variation, hardness, dissolution, and in vitro drug release. This foundational knowledge is critical for ensuring the safety, efficacy, and stability of aspirin as a widely used therapeutic agent.

1.Introduction

Anti-inflammatory drugs are a class of medications used to reduce or alleviate inflammation in the body. Inflammation is a natural response by the body's immune system to injury, infection, or irritation.

These drugs work by targeting the processes that cause inflammation, such as the production of inflammatory chemicals (like prostaglandins) or the activity of immune cells involved in the inflammatory response.

2.Classification

Anti-inflammatory drugs are mainly classified as:

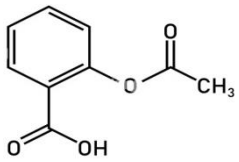
1.Non-Steroidal Anti-Inflammatory Drugs

Example: Aspirin, ibuprofen, diclofenac, celecoxib etc.

2.Steroidal Anti-Inflammatory Drugs

Example: Dexamethasone, prednisone.

ASPIRIN



$C_9H_8O_4$

- **IUPAC Name:** 2-acetoxybenzoic acid
- **Molecular Formula:** C9H8O4
- **Molecular Weight:** 180.16 g/mol
- **Structure:** Consists of a benzene ring with an ester group (acetyl) and a carboxylic acid group (COOH)

3.Available dosage form

Dosage Form	*Route*	*Common Strengths*	*Examples (Brand Names)*	*Main Use*
Plain Tablets	Oral	300 mg, 325 mg, 500 mg	Disprin®, Aspro®, Bayer® Aspirin	Pain, fever, inflammation
Enteric-Coated Tablets	Oral	75 mg, 81 mg, 100 mg, 325 mg	Ecosprin® (India), Ecotrin®, Cardiprin®	Antiplatelet (cardioprotection)
Chewable Tablets	Oral	81 mg	St. Joseph® Aspirin, Bayer® Chewable	Emergency MI, stroke prevention
Effervescent Tablets	Oral (dissolved in water)	325 mg, 500 mg	Alka-Seltzer® (aspirin + antacid), Disprin®	Headache, cold relief, gastric-friendly
Suppositories	Rectal	300 mg, 600 mg	Generic formulations	When oral route is not possible
Extended-Release Tablets	Oral	81 mg, 325 mg	Aspirin 81 mg ER, Durlaza® (US)	24-hour antiplatelet action
Gum / Lozenges (rare)	Buccal	227 mg (in combo)	Aspergum® (discontinued in many regions)	Mild pain, sore throat (old formulation)
Topical (as salicylates)	Topical (skin)	N/A (not pure aspirin)	Bengay®, IcyHot®, Salonpas®	Local muscle/joint pain (methyl salicylate)

4.Preformulation studies

Preformulation studies are the initial investigations performed on an active pharmaceutical ingredient (API) to collect critical information regarding its **physical, chemical, mechanical, and biological characteristics**.

4.1 Organoleptic Properties of Aspirin

Property	**Observation**	**Importance**
Color	White or off-white crystalline powder	Visual identification & purity
Odor	Faint vinegar-like smell	Detects degradation (acetic acid smell = hydrolysis)
Taste	Bitter	May require taste masking in chewables/suspensions

4.2 Physical Properties

*A) **Melting Point***

- *Observed at ~136°C*
- Sharp melting point = *pure substance*
- Broader/lowered melting = *impurities or polymorphs*

*B) **Hygroscopicity***

- Aspirin absorbs moisture easily → undergoes hydrolysis
- *Tested by*: placing aspirin in humid environments and observing weight changes
- *Result*: Needs packaging with *desiccants, foil strips, or blister packs*

4.3 Micromeritic Properties

A) **Bulk Density***:*

- Measured using a *graduated cylinder*. It's an important factor because it influences *uniform tablet filling*.
- For aspirin tablets, a *bulk density* of 0.4–0.6 g/cm³ is ideal for *tablet compression*.

B) **Tapped Density:**

- Determined by *tapping the powder* to assess how much the powder settles when subjected to vibration.
- This helps calculate the *compressibility index* (Carr's Index) and *Hausner ratio*, which determine how well the powder will compress into

tablets.

Property	Value	Significance
Angle of Repose	<30° (ideal)	Good flow
Carr's Index	<15%	Good compressibility
Hausner's Ratio	<1.25	Acceptable flow

4.4 Chemical Properties

A) **pKa (≈ 3.5)**

- Indicates aspirin is a *weak acid*
- In stomach (acidic): less ionized → *poor solubility, better absorption*
- In intestine (alkaline): more ionized → *better solubility, poor absorption*
- Helps design *enteric-coated tablets* that dissolve in the intestine.

B) **Partition Coefficient (Log P ≈ 1.2)**

- Shows *moderate lipophilicity*
- Indicates it can cross membranes by passive diffusion → good *oral absorption*

4.5 stability study of aspirin

A) hydrolytic stability

- *Test:* Tablets stored at high humidity (75% RH) at 40°C for 3 months.
- *Observation:* Aspirin degraded into salicylic acid and acetic acid.
- *Result:* 5–10% degradation noted after 90 days.

B) *Thermal Stability*

- *Test:* Tablets stored at 50°C for 1 month.
- *Observation:* Slight discoloration and 3–6% degradation observed.
- *Result:* Potency reduced after prolonged exposure.

C) Photostability

- *Test:* Exposed to fluorescent light (1.2 million lux hours).
- *Observation:* Minor degradation (<2%) detected.

Stability Studies (ICH Guidelines)

Conditions tested:

Type	Conditions
Accelerated	40°C / 75% RH
Intermediate	30°C / 65% RH
Long-term	25°C / 60% RH

FORMULATION OF ASPIRIN TABLET

Core Composition

Ingredients	Quantity per tablet	Function
Aspirin	325mg	API
Lactose monohydrate	100mg	Diluent
Microcrystalline cellulose (avicel Ph 101)	60mg	Binder and disintegrant
Corn starch(pregelatinized)	30mg	disintegrant

Povidone (PVP K30)	10mg	Binder
Magnesium stereate	4mg	Lubricant
Talc	6mg	Glidant

Enteric coating composition:

Ingredients	**Quantity per tablet**	**Function**
Cellulose acetate phthalate	10mg	Enteric polymer
Diethyl phthalate (plasticizer)	2mg	Improve film flexibility
Talc	3mg	Prevent sticking during coating

Manufacturing of Enteric-Coated Aspirin Tablets

1. Core Tablet Preparation (Wet Granulation Method)

- *Weigh and sieve* aspirin and excipients (e.g., lactose, starch, MCC).
- *Dry mix* all ingredients uniformly.
- Prepare *PVP binder solution* in isopropyl alcohol.
- *Granulate* the powder with binder to form a wet mass.
- *Screen* through a #16 mesh to form granules.
- *Dry* the granules at 40–50°C.
- *Sieve* dried granules through #20 mesh.
- *Lubricate* with talc and magnesium stearate.
- *Compress* into tablets (~535 mg/tablet).

2. Enteric Coating

- Prepare coating solution with *cellulose acetate phthalate (CAP)*, *plasticizer*, and *talc* in organic solvent.
- *Coat tablets* in a pan coater or fluidized bed coater.
- Dry coated tablets to remove solvent.
- Coating weight gain: *~5%*

EVALUATION OF ASPIRIN TABLET

The evaluation of aspirin tablets is a crucial step in ensuring their quality, safety, and efficacy. After formulation and manufacturing, tablets must meet specific pharmacopoeial standards and quality control parameters before they can be approved for use. These evaluations are essential to confirm that the tablets possess the desired physical and chemical characteristics, such as uniform weight, appropriate hardness, disintegration time, and accurate drug content.

1.WEIGHT VARIATION:

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 (Sartorious GmbH type A 6801) and compared with permissible limits.

Average Weight of Tablet	Maximum % Deviation Allowed	Max Tablets Outside Limit
≤ 80 mg	±10%	Not more than 2
> 80 mg and < 250 mg	±7.5%	Not more than 2
≥ 250 mg	±5%	Not more than 2

Friability: Friability test was preformed 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, 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.

Friability (%)	**Interpretation**
≤ 1.0%	Acceptable
> 1.0%	Tablet may be too fragile
< 0.5%	Very good mechanical strength

2.HARDNESS:

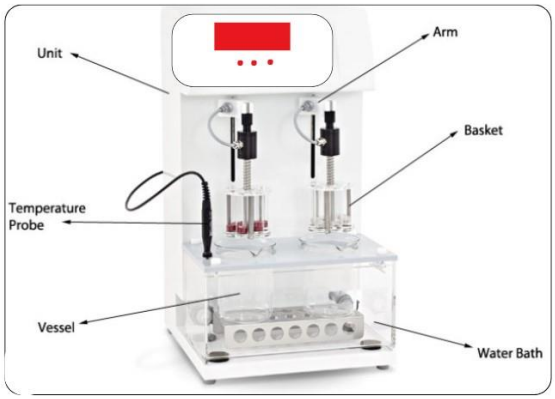
Tablet requires a certain amount of strength or hardness and resistance to friability to withstand mechanical shakes during handling in the manufacture, packaging, and shipping. Hardness generally measures the tablet crushing strength. The hardness of tablets was determining Pfizer hardness tester. Hardness of randomly selected 10 tablets of each brand and trial formulation batch was measured using Hardness Tester Load was given to tablets in a diametric direction to determine an actual load when the tablet was broken.

Tablet type	Tablet hardness
Uncoated aspirin tablet	4 – 6 kg/cm² (approx. 40–60 N)
Enteric coated aspirin tablet	*5 – 8 kg/cm²* (approx. *50–80 N*)

3.DISINTEGRATION TIME:

The U.S.P. device to test disintegration consists of 6 glass tubes that are 3inchlong; open at the top and 10 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 either water, simulated gastric fluid or simulated intestinal fluid at 37 ± 2 °C such that the tablet remains 2.5 cm below the surface of liquid on their upward movement and not closer than 2.5 cm from the bottom of the beaker in their downward movement. Move the basket containing the tablets up and down through 5-6 cm at a frequencyof 28 to 32 cycles per minute.

Tablet Type	Test Stage	Medium	Temperature	Time Limit	Acceptance Criteria
Enteric-Coated Tablet	Stage 1: Acid Resistance	0.1 N HCl (Simulated gastric fluid)	37 ± 2°C	2 hours	No disintegration, cracking, or softening in all 6 tablets
	Stage 2: Buffer Stage	Phosphate buffer pH 6.8	37 ± 2°C	Within 60 minutes	All 6 must disintegrate completely; 16 of 18 must pass if retested



4.DRUG CONTENT:

The tablets were powdered, and 250 mg equivalent weight of aspirin in tablet powder was accurately weighed and transferred to a 100-ml volumetric flask. Initially, 10 ml of phosphate buffer (pH 7.2) was added and shaken for 10 min. Thereafter, the volume was made up to 100 ml with buffer. Subsequently, the solution in the volumetric flask was filtered, and 1ml of the filtrate was diluted and analyzed at 265 nm using UV-visible spectrophotometer.

%Drug Content= (Standard absorbance or peak areas ample absorbance or peak area)×Label claim

- **Acceptance Range (as per USP/IP/BP)**:
- **Not less than 95%** and **not more than 105%** of the labeled amount.

5.DISSOLUTION TEST:

Dissolution of commercially available brands and formulated aspirin tabletswas 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.

Stage	Medium	Duration	Limit
Acid Stage	0.1N HCl (pH 1.2)	2 hours	≤ **10%** release
Buffer Stage	pH 6.8 buffer	Within 45 min	≥ **80%** release

6.ASSAY:

Twenty tablets were accurately weighed and then 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 then 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.

❖ Acceptable Range:
Not less than 95.0%
Not more than 105.0%

7.IN VITRO DRUG RELEASE STUDY:

The release rate of Aspirin from tablets was determined using United States Pharmacopeia (USP) Dissolution Testing Apparatus Type-II. The dissolution test was performed using 900ml of 5.8pH phosphate buffer, at 37ºC±0.5ºC and 50 rpm. A sample (10ml) of the solution was withdrawn from the dissolution apparatus hourly and the samples were replaced with fresh dissolution medium. The samples were filtered through a 0.45µ membrane filter. Absorbance of these solutions was measured at 265 nm using a Thermospectronic-1 UV/V double-beam spectrophotometer.

Phase	Medium	Duration	Limit
Acid Stage	0.1N HCl (pH 1.2)	2 hours	≤ **10%** release
Buffer Stage	pH 6.8 buffer	Within 45 min	≥ **80%** release

CONCLUSION

This article provides a comprehensive overview of aspirin, a widely used non-steroidal anti-inflammatory drug (NSAID) known for its analgesic, antipyretic, anti-inflammatory, and antiplatelet properties. It explores aspirin's classification, chemical structure, and various dosage forms, with a focus on the development of enteric-coated tablets. Detailed preformulation studies highlight the importance of physical, chemical, and micromeritic properties, as well as stability concerns related to moisture and temperature. The formulation process using wet granulation and enteric coating is thoroughly described, along with evaluation parameters such as weight variation, friability, hardness, disintegration time, drug content, dissolution, assay, and in vitro drug release. These assessments are essential to ensure the quality, safety, and therapeutic effectiveness of aspirin. In conclusion, aspirin remains a vital therapeutic agent, and careful attention to formulation and evaluation is crucial in maintaining its efficacy and stability for a wide range of clinical uses.

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