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Biological Activities and Industrial Production of Aspirin (Acetylsalicylic Acid)

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Abstract

Aspirin (acetylsalicylic acid) naturally originates from a glycoside known as salicin and is essentially regarded as the oldest and most widely used drug in the world. The demand for aspirin as an effective drug in the pharmaceutical industry is in the increased. Medically, the drug has been spotted as one that is effective in ameliorating fever, general pain and inflammation. It has both ester and carboxylic acid functional groups. Industrially produced aspirin mainly comes in different forms; tablets, capsules and liquid elixir. The tablet form is the most common and is the subject of this review. This review looks at the chemistry of aspirin, it functions in the human body as a bioactive compound and how it is produced industrially. Key Words: Aspirin, Biological, Industrial, ester, carboxylic acid analgesic, antipyretic, anti-inflammation.

INTRODUCTION

In connection to the study, a drug is any chemical substance given to treat or prevent sickness. An estimated $6 billion is spent worldwide each year on analgesic, antipyretic and anti-inflammation drugs and aspirin is no exception [1]. Aspirin is a derivative of salicylic acid used medicinally to reduce fever, inflammation, prevent blood clots and strokes, and relieve mild and chronic post-surgery pain [2]. Aspirin as a therapeutic agent gained astronomical attention in the fifteenth century when Hippocrates used extracts of the bark and leaves of willow tree to relieve pain and fever. Synthesis of salicylic acid and the production of aspirin by various scientists began in the

1800s [3]. Bayer of France was the first to market the powder form of aspirin until 1899[3; 4]. An estimated 120 billion aspirin tablets are taken yearly placing it among the top three most used drugs in the world [5].With the growing demand of aspirin, there is need to synthesize it in large quantities; thus its industrial preparation. This paper will serve as a reference material for undergraduate students in organic chemistry, industrial chemistry and its related areas.

CHEMISTRY OF ASPIRIN

Aspirin is a class of chemical compound with a formula weight of 180.16gmol^{-1} and chemically related to acetaminophen having a molecular formula of $HC_9H_7O_4$ [6]. In its synthetic form, aspirin looks white crystalline powder with no definite smell [7], however, when exposed to the atmosphere, it slowly hydrolyses and acquires odor like vinegar [7; 8]. Aspirin has a half-life of about one hour in the human plasma and a pKa value of 3.7[9]. It is an aromatic compound with both ester and carboxylic acid functional groups [6]. It is considered a weak acid and sparingly soluble in water, but more readily soluble in basic medium [6]. Aspirin is stable, nonhygroscopic solid with low melting point of 138-140^{0}C and a density of 1.40gcm^{-3} [6; 7; 9].

BIOLOGICAL ACTIVITIES OF ASPIRIN

First the paper examines how aspirin is digested, distributed, metabolized and excreted from the human body. Aspirin is readily soluble in basic medium; as a result, it is quickly digested in the small intestine by inactively intermingling with the body fluid and bio transformed to salicylate in the liver and intestine [6; 10]. It is quickly distributed in to the blood fluid compartments and binds to the albumin in the blood plasma and later reaches the bone marrow megakaryocytes where it inhibits COX-1 and COX-2 [10]. It is easily expel from the body through excretion. Aspirin works by weakening the hormones and inhibiting the growth of cells that cause pain and inflammation [10; 11]. It achieves this by inhibiting the synthesis of the prostaglandins which are lipids derived from prostanoic acid that transfer pain messages to the brain [2; 11]. Extensive research has been done on the pharmacokinetics and biological activities of aspirin and conclusions drawn labeling it as an active antiplatelet agent used in the prevention of heart attack, strokes, fever, arthritis and myocardial infraction [2; 11]. Aspirin plays a crucial role in tackling old-diseases because of its antioxidant, antiplatelet and anticoagulant effects. When taken in low dose, aspirin is reported to be an effective anti-coaggregatory [11]. Regular oral administration of aspirin is said to retard the development of coronary arteries disease [12]. Recent clinical trials have shown that regular

administration of aspirin is effective in preventing and lowering the risk of colorectal and gastrointestinal cancer [13], it also reduces the mortality rate of breast cancer. It does this through biological mechanisms; inhibits COX-2 Pathways, acts as antiplatelet agent [13].

Common side effects of aspirin includes; skin rashes for allergic patients, abdominal pain, gastrointestinal bleeding, stomach upsets, heartburn, drowsiness, headache, nausea and bleeding [14; 15]. Naturally active and safe alternatives of aspirin includes; extracts from the bark and leaves of willow tree, leafy green vegetables and fruits, ginger, nuts and seeds, turmeric, foods reach in magnesium and Methylsulfonylmethane-an active herb that tackles stress and heal wounds [5].

INDUSTRIAL PRODUCTION OF ASPIRIN

The industrial production of aspirin is a simple method compared to other drugs [3]. However, the manufacturing process of aspirin tablets varies in different pharmaceutical companies in terms of size, shape, hardness, weight and thickness [3]. Since the method of production is the same, product yield will not vary considerably. The production of aspirin has land mark advancement in the pharmaceutical industry. With the growing importance of technological advancement, the production of aspirin is highly automated and computerized in most pharmaceutical companies [3].

Raw Materials

1. Acetylsalicylic acid- the active ingredient
2. Corn starch
3. Cold Purified Water
4. Lubricant (e.g. Hydrogenated vegetable oil, stearic acid, talc, or aluminum stearate)
5. Diluents (mannitol, lactose, sorbitol, sucrose or inositol)
6. Flavor agents (saccharin)
7. Coloring agents (iron oxides, FD&C Yellow No. 5, FD&C Yellow No. 6, FD&C Red No.3, FD&C Red No. 40, FD&C Blue No.1, FD&C Blue No. 2, FD&C Green No.3 and a limited number of D&C colorants)[3].

Manufacturing Process

The manufacturing process of aspirin involves seven main steps: weighing; mixing; dry screening; compression; testing; quality control, and bottling & packaging. These steps are described hereunder:

1. **Weighing**. Weight the desired amount of the corn starch, the active ingredient, water and the lubricant in separate sterile canisters.

2. **Mixing**. Mix the corn starch with purified cold water and stir to obtain a translucent paste. Next mix the translucent paste, the active ingredient, lubricant and diluent in a sterile canister, transfer the mixture to the Glen Mixer and mix continuously until a homogenous mixture is obtained with no air bubbles. The Gel Mixer will mechanically separate the mixture in to units and desired slugs. The active ingredient helps to bind the mixture together, diluent makes the slugs expand and the lubricant prevents the mixture from sticking to the machine [3]

3. **Dry Screening**. Use a stainless steel spatula to introduce the slugs to the Fitzpatrick Mill and add more lubricant. The Fitzpatrick Mill will blend the mixture gently while the lubricant further prevents the slugs from sticking in the granulator and sifter [3].

4. **Compression:**

I. Use a single-punch to feed the mixture in to the dye cavity through a feed shoe, then use a sizable rod steel to compress the slugs in to tablets. When completely compressed, the tablets are ejected through the dye cavity. This is only applicable to small scale production [3].

II. For rotary tablet machine, feed the mixture in to several dye cavities connected to a large steel plate. While the steel plate rotates, the mixture is distributed to the feed line which supplies each dye cavity with the mixture. The rotation continues until all dye cavities are completely filled with the mixture. Then on the upper side of each cavity, the roller above presses the mixture in each dye cavity to compress them in to tablets, while the roller beneath each dye cavity

lifts up to eject the tablets from the dye platform [3]. This method of compression is desired for large scale production of aspirin tablets.

5. **Testing.** Once produced, use Schleuniger or Herberlein and Roche Friabilator to test for the hardness and friability of the tablets respectively. These tests are done to ensure that the tablets do not break under normal conditions and can resist rigorous packaging and transportation [3].

6. **Quality Control**. According to the Food and Drug Administration (FDA), all equipment and machines should be sterilized before production process begins.

Quality control is done to ensure that the tablets are not contaminated and parameters such as hardness, weight, friability, disintegration time and dissolution time are maintained. With a mesh screen, periodic checks, disintegration tests and batch records are done to maintain accurate and dosage amount throughout the manufacturing process. The disintegration test is done to ensure that the tablets will dissolve in water at the desirable rate with a suitable temperature of about 2.77^0C [3].

7. **Bottling and Packaging**. Bottle the tablets with a polypropylene plastic bottles or glass amber bottles through an automated bottling assembly line. Stopper the bottles with a cotton packaging, seal the top with shear aluminum and finally with plastic and rubber child-proof lid, then support the stopper with a round plastic band. Label the bottles with manufacturer name, dosage amount, manufacturing and expiration dates. Package the bottles in large cartons for shipping and distribution [3]. The choice of bottles is essential in preserving the tablets for long time. Such kind of bottles also helps to prevent the rays of the sun from reaching the tablets.

DOSAGE AMOUNT OF ASPIRIN

Review of data published by the World Health Organisation Essential Medicine List on dosage strengths places the dosage amount of aspirin at 100mg and 500mg [16]. Dosage strengths of 50mg to 500mg and 81mg to 500mg are often used in the United States and Germany respectively [17]. This range of dosage amounts is what is prescribed for patients needing aspirin. Approximately one tablet of aspirin a day can arrest cerebral thromboses; two to six tablets a day can lessen general body pain [3].

CONCLUSION

The pharmacokinetics and biological activities of aspirin have made it gained a wide range of acceptance in to the pharmaceutical industry thus the need to produce it in large scale. This wonder drug continues to play a leading role in the medical field as an effective antipyretic, analgesic and anti-inflammation agent. Industrial production of aspirin is simple, less time consuming and a lucrative enterprise. The four raw materials; acetylsalicylic acid, corn starch, lubricant (hydrogenated vegetable oil) and diluents (mannitol) are readily available.

RECOMMENDATIONS

The drug produced is of immense medical use and it is encouraged that the drug is used for analgesic, antipyretic, anti-inflammation and cardiovascular related problems.

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