Microwav Assisted Green Synthesis of Paracetamol, Aspirin and their Pharmacokinetic Studies

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Abstract: **The research looks at a new way to make Paracetamol and Aspirin using green chemistry concepts via solvent free reaction and under microwave irradiation. The synthesis was carried out from salicylic acid and 4- aminophenol, acetic anhydride, and no catalyst. The reaction time for both the molecules was low. The yield of Paracetamolis 92.0% and Aspirin is 82.0%. The reaction progression was confirmed by TLC. The structure of the compounds was confirmed by FT-IR and Melting point. Upon literature studies, our work was focussed on the biological metabolismof these synthesized compounds. The compounds were tested for pharmacological studies. We reported the pharmacokinetics and their side effects during the metabolism in the human body. The results were interpreted.**

Key Words: Paracetamol, Aspirin, Microwave method, Green Chemistry, Pharmacokinetics.

I. INTRODUCTION

Today, Paracetamol is a widely used drug in many nations and pharmaceutical formulations. Its composition drugs are used to treat and/or relieve minor aches and pains [1] and are used for cold and flu Infections due to their antipyretic activity[2].

It is also used to treat and relieve severe pain like post-operative pain [3] and palliative care for cancer patients. Therefore, we planned for the synthesis of this drug by green chemistry. Microwave method is a suitable method for green synthesis. 4-amino phenol treated with acetic anhydride inacidic media to form paracetamol [4-5].

Figure 1 shows the chemical structures of Paracetamol (PAR) and Aspirin (ASA).

The scope for this drug led to the manufacture of active pharmaceutical ingredients and statistics showing that over 1, 45,000 tonnes of paracetamol were synthesized every year. Green chemistry is a challenging task to follow the synthetic procedures. It is an "Engineering idea" of pollution prevention and zero waste. It also promotes the adoption of cost favor andenvironmental friendly methods.

The literature study shows that Aspirin is a very scope drug in the field of medical science [6-7]. After literature survey, we planned to work on the synthesis of Aspirin. Aspirin is known as Salicylates. It is a common drug used for minor aches, pains and fevers. It shows anti-inflammatory activity. In this work, we synthesized the drug by salicylic acid under microwave irradiation [8]. After the synthesis, we tested its pharmacokinetics and for side effects. The metabolism studies have been done.

II. MATERIALS AND METHODS

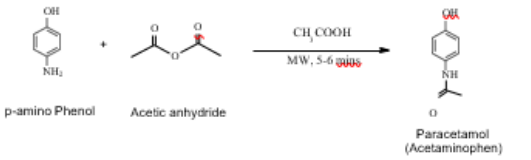
All required Chemicals are purchased from Davangere Scientifics. The reaction was carried in Microwave Oven (Convention) (20L, 23,500MHz). The TLC was checked in UV-Chamber and Iodine Chamber. The molecules were characterized by FT-IR (Bruker) in SJMIT, Chitradurga. Pharmacokinetic studies in SS research centre.

A. Experimental Section:

General Procedure for the synthesis of Paracetamol: The solid 4-amino Phenol (10 Mmol) was added with aceticanhydride (10 Mmol) in an acidic medium. The sealed reaction mixture was kept in microwave oven for the reaction to proceed. The progress of the reaction was confirmed byTLC. After the reaction, the solution turns to white solid precipitate. The crude solid was recrystallized by ethanoland water. The product was purified by washing with waterfor 2-3 times, filtered and dried.

General Procedure for the synthesis of Aspirin: The Salicylic acid solution (10 Mmol) was added with acetic anhydride (10 Mmol) in an acidic medium. Microwave oven was subjected to the reaction by inserting the reaction mixture into it. The confirmation of the reaction was done by TLC. After the reaction completion, the solution turns to white solid. The crude white was recrystallized by ethanol and water. The product was purified by water wash for 2-3 times. The solution was filtered and dried (Fig-2).

Scheme-1: Synthesis of Paracetamol and Aspirin under Microwave irradiation



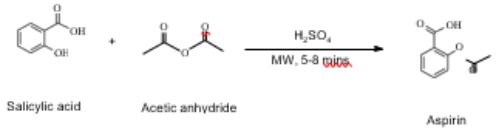


Fig-2: Synthesis of Paracetamol and Aspirin

III. SPECTRAL DATA FT-IR

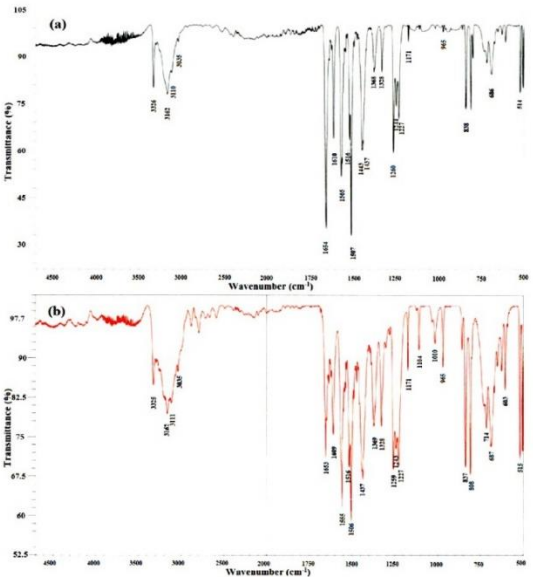


Fig-3: FT-IR of Paracetamol

FT-IR (KBr) υ cm^{-1}: 3325 (-OH stretching), 3162-3035 (CH_3 stretching), 1665 (C=O, Amide), 1609 (C=C) (Fig-3)

Aspirin

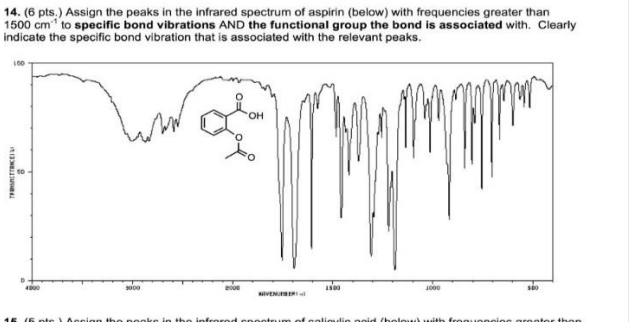


Fig-4: FT-IR of Aspirin

FT-IR (KBr): υ cm^{-1} 3000 (O=C-OH, carboxylic), 1757 (-O-
C=O, Ester) (Fig-4).

IV. PHARMACOKINETICS AND SIDE EFFECTS:

PARACETAMOL

The maximum single-dose of acetaminophen for pain or fever is 1,000 mg every 4 hours as needed, up to a maximum daily intake of 4g. The therapeutic concentrations range from 5 to 20 mg/ml (Table-1). The plasma maximum concentration (Cmax) is 12.3 g/ml after oral administration of 1,000 mg acetaminophen, the area under the curve over 6 h AUC (0–6) is 29.4 g/h/ml, and the AUC extrapolated to infinity (AUC0–) is 44.4 g/h/ml (Bertolini et al., 2006) [9-11].

The elimination half-life (t1/2) is 2.53 hours, and the time to peak concentration (Tmax) is 1.0 hour. These findings demonstrate that intravenous acetaminophen delivery results in higher peak plasma levels and occurs sooner than oral dosing [12-15].

Aspirin

Table-1: Pharmacokinetic parameters

Oral Bioavailability (F)	65%
Clearance (CL)	33 L
Volume of distribution (Vd)	9.0L
Half-life ($t_{1/2}$)	0.25h

CONCLUSION:

Both Paracetamol and Aspirin synthesized by Green Chemistry. Pharmacokinetic studies were evaluated and reported their side effects. Overall studies concluded that drugs can be synthesized by green route under microwave method. Also, drugs are having cytotoxic effects for human.

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