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# Detection of chemical drug adulterants in herbal supplements: A GC-MS identification of paracetamol, prednisone, and prednisolone

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## ABSTRACT

**Background:** Traditional Medicine and Health Supplements are products intended to provide health benefits because they are made based on herbal ingredients that do not contain Chemical Drugs (BKO), but sometimes there are some BKO detected in Traditional Medicine and Health Supplements such as Paracetamol, Prednisone, and Prednisolone. **Methods:** Identification of the three compounds was carried out using the Gas Chromatography Mass Spectrometry method. Sample codes 0014A and 0014B have retention times and areas that are not the same as the standard solutions of the three compounds. **Findings:** The presence of these three compounds makes Traditional Medicine and Health Supplements dangerous if they exceed the specified requirements. **Conclusion:** The identification results of Paracetamol show a retention time value of 9,559 and an area of 169 for sample code 0014A, in sample 0014B no retention time and area were detected. In the identification of Prednisone and Prednisolone, both samples 0014A and 0014B no retention time and area were detected, so it can be said that the samples meet the requirements and are suitable for consumption by the public. **Novelty/Originality of this article:** Based on the analysis method (103/OTSK/MA-PPPOMN/20) states that the determination of the detection limit (LOD) for Paracetamol is 4.32 µg/g (solid preparation) and 2.02 µg/mL (liquid preparation), for Prednisone is 25.18 µg/g (solid preparation) and 11.78 µg/mL (liquid preparation), and Prednisolone is 86.86 µg/g (solid preparation) and 40.63 µg/mL (liquid preparation).

**KEYWORDS**: gas chromatography mass spectrometry; health supplements; paracetamol; prednisolone; prednisone; traditional medicine.

## 1. Introduction

The Food and Drug Supervisory Agency/*Badan Pengawas Obat dan Makanan Republik Indonesia* (BPOM) was established during the Dutch colonial era under the name De Dient Van De Valks Gezonheid (DVG). DVG was established under a Dutch pharmaceutical company whose function was to make chemical drugs and a pharmaceutical research center. Entering the phase of Indonesian independence, the DVG company was taken over by Indonesia. In 1964, DVG was changed to the Pharmaceutical Inspectorate and three years later the name of the Pharmaceutical Inspectorate changed to the Pharmaceutical Affairs Inspectorate. In 1976 there was another internal reshuffle and its name changed to the Directorate General of Pharmacy. In its working mechanism, the Directorate General of

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Pharmacy cooperates with related agencies, namely the National Pharmaceutical Institute, the Ministry of Health, and the State Pharmaceutical Industry in matters of drug and food supervision.

The Food and Drug Supervisory Agency/*Badan Pengawas Obat dan Makanan Republik Indonesia* (BPOM) was initially under the Ministry of Health of the Republic of Indonesia as the Directorate General of Drug and Food Supervision with the main task of implementing the regulation and supervision of drugs, food, cosmetics, and medical devices, traditional medicines, narcotics and hazardous materials (Rabbany, 2023) . Based on Presidential Decree No. 16 of 2000 which was later changed to Presidential Decree No. 103 of 2001 concerning the Position, Duties, Functions, Authorities, Organizational Structure, and Work Procedures of Non-Departmental Government Institutions, BPOM was designated as a Non-Departmental Institution/*Lembaga Pemerintah Nondepartemen* (LPND). LPND was then changed to a Non-Ministerial Government Institution/*Lembaga Pemerintah Nonkementerian* (LPNK) based on the Law of the Republic of Indonesia Number 39 of 2008 concerning the State Ministry. Based on the laws and regulations as mentioned above, the position of BPOM is as follows: BPOM is a Non-Ministerial Government Institution formed to carry out certain government tasks from the president. BPOM is under and responsible to the President. In carrying out its duties, BPOM is coordinated by the Minister of Health. BPOM is led by the Head of the Agency.

*1.2 The food and drug monitoring center in Denpasar*

The Food and Drug Supervisory Agency/*Badan Pengawas Obat dan Makanan Republik Indonesia* (BPOM) in Denpasar is one of the Technical Implementation Units/*Unit Pelaksana Teknis* (UPT) within the POM Agency which was established based on the Decree of the Head of POM Agency Number 05018/SK/KBPOM in 2001 concerning the Organization and Work Procedures of UPT within the POM Agency. BPOM in Denpasar as a Technical Implementation Unit/*Unit Pelaksana Teknis* (UPT) within the POM Agency has an important role as an extension of the POM Agency, namely implementing policies in the field of supervision of therapeutic products, narcotics, psychotropics and other addictive substances, traditional medicines, cosmetics, complementary products, food safety and hazardous materials in the Bali Province. The Center for Drug and Food Control (BBPOM) in Denpasar as the Technical Implementation Unit of BPOM RI in Bali Province carries out drug and food supervision based on the vision and mission of BPOM RI as the parent institution, the Vision and Mission of BPOM is stipulated in the Regulation of the Head of BPOM. BPOM's Vision: "Safe, quality, and competitive drugs and food to realize a sovereign, independent, and individualistic Indonesia based on mutual cooperation." BPOM's Mission: Building superior human resources related to Drugs and Food by developing partnerships with all components of the nation in order to improve the quality of Indonesian people. Facilitating the acceleration of the development of the Drug and Food business world by siding with MSMEs in order to build a productive and competitive economic structure for national independence. Increasing the effectiveness of Drug and Food supervision and the prosecution of Drug and Food crimes through synergy between the central and regional governments within the framework of the Unitary State for the protection of the entire nation and to provide a sense of security to all citizens. Clean, effective, and trusted government management to provide excellent public services in the field of Drugs and Food.

*1.3 Main duties and functions of the food and drug monitoring center in Denpasar*

Based on Article 3 of BPOM Regulation No. 12 of 2018, the POM Center in Denpasar as one of the Technical Implementation Units of BPOM has the task of implementing technical operational policies in the field of Drug and Food Supervision which includes supervision of therapeutic products, narcotics, psychotropics, addictive substances, traditional medicines, cosmetics, complementary products, as well as supervision of food safety and hazardous materials in accordance with the provisions of laws and regulations. In carrying out its

duties, the POM Center in Denpasar as one of the UPTs within The Food and Drug Supervisory Agency/*Badan Pengawas Obat dan Makanan Republik Indonesia* (BPOM) carries out the following functions: Preparation of plans and programs in the field of Drug and Food supervision. Implementation of inspections of Drug and Food production facilities. Implementation of inspections of Drug and Food distribution facilities and/or pharmaceutical service facilities. Implementation of product certification and production facilities and/or distribution of Drug and Food. Implementation of sampling, on-site inspections, and inspections of production and distribution facilities. Implementation of Drug and Food testing. Implementation of intelligence and investigation into violations of provisions of laws and regulations in the field of Drug and Food supervision. Implementation of communication, information and education and public complaints in the field of Drug and Food supervision. Implementation of coordination and cooperation in the field of Drug and Food supervision. Implementation of monitoring, evaluation, and reporting in the field of Drug and Food supervision. Implementation of administrative and household affairs. Implementation of other functions assigned by the Head of the Agency.

*1.5 Organizational culture of the food and drug monitoring center in Denpasar*

Organizational culture is the noble values that must be believed, internalized and practiced by all members of the organization in carrying out their duties. The organizational culture of the POM Center in Denpasar is developed with noble values.

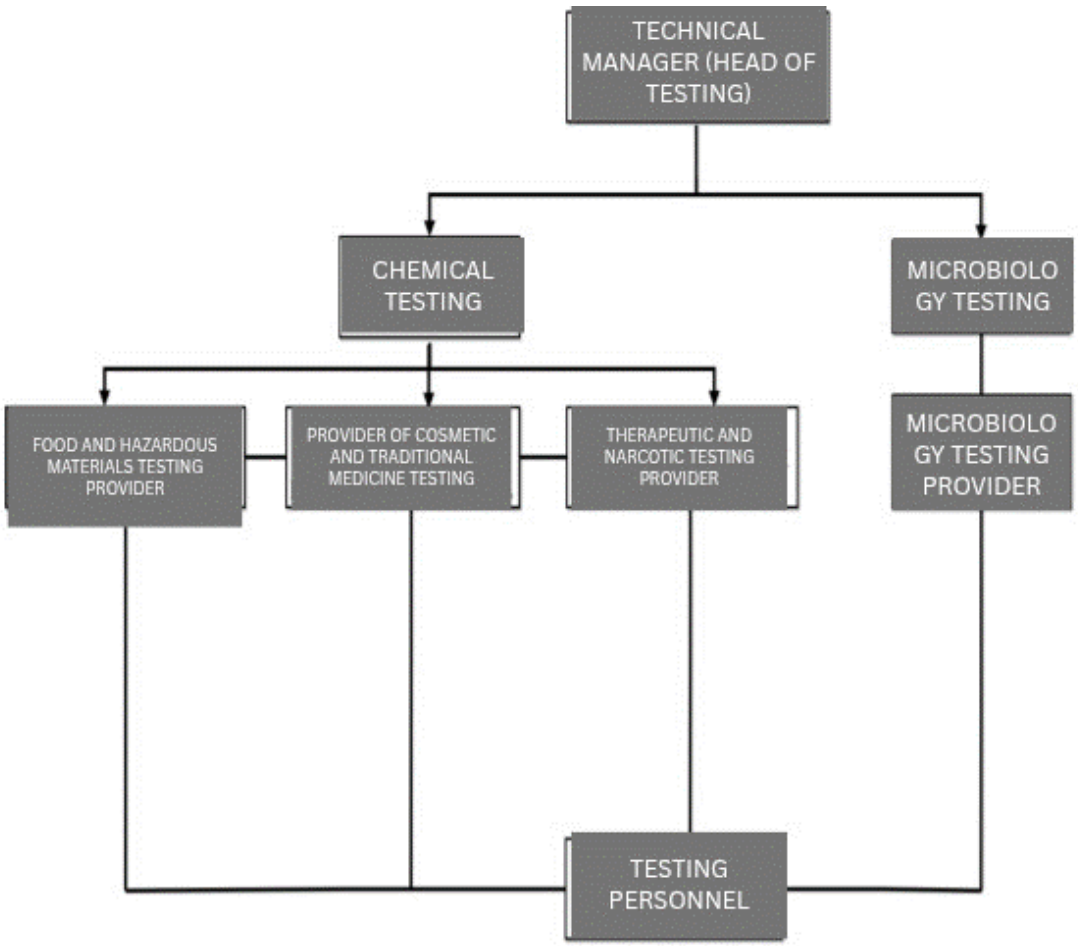


Fig 2. Laboratory management system of the POM center in Denpasar

Professional: Upholding professionalism with integrity, objectivity, perseverance and high commitment. Integrity: Consistency with unshakable steadfastness in upholding noble values and beliefs. Credibility: Trustworthy and recognized by the wider community,

nationally and internationally. Teamwork: Prioritizing openness, mutual trust and good communication. Innovative: Able to make innovations in accordance with the latest science and innovation. Responsive or responsive: Anticipating and being responsive in solving problems. All laboratory testing activities at the POM Center in Denpasar are headed by a head of testing or referred to as a technical manager based on the quality management system. Laboratory management at the POM Center in Denpasar can be described as in Figure 2. Testing activities at the POM Center in Denpasar are divided into two, namely chemical testing and microbiological testing. Chemical testing has 3 laboratories, namely the food and hazardous materials testing laboratory, the cosmetics and traditional medicine testing laboratory and the therapeutic and narcotics testing laboratory. Furthermore, microbiological testing only has one laboratory, namely the microbiology laboratory. Each laboratory is appointed by a supervisor who is responsible for supervising testing and administration activities in each laboratory. Testing activities in each laboratory are carried out by testing personnel.

## 2. Methods

Analysis of paracetamol, prednisone, and prednisolone in traditional medicines and health supplements was carried out using the separation method using Gas Chromatography–Mass Spectrometry based on the analysis method 103/OTSK/MA-PPPOMN/20. The materials used as samples are traditional medicines and health supplements. Samples were obtained from third parties received in September 2022 by the Center for Drug and Food Control in Denpasar. The chemicals used are comparative standards from BPFI paracetamol, BPFI prednisone, and BPFI prednisolone. The reagents used were mineral-free water, ammonia, ether, methanol, and two solutions made, namely 1 N sodium hydroxide solution and 1 N hydrochloric acid solution. The tools used are a set of gas chromatography equipment equipped with a capillary column containing 5% Diphenyl/95% Dimethylpolysiloxan (0.25 mm × 30 m, 0.25 μm), and a Mass Spectro detector, sonicator, vortex, centrifuge, centrifuge tube.

### *2..1 Preparation of test solution*

Test solution 1, the average weight was determined first on 10 packs/capsules/tablets/liquids and homogenized. Weighed or pipetted an amount of 1 dose of traditional medicine/health supplement and put into a 50 mL centrifuge tube, added 50 mL of mineral-free water, basen with 1 N sodium hydroxide solution to pH 10-11, then shaken for 30 minutes. The solution was filtered or centrifuged until a precipitate and clear solution were obtained at a speed of 3500 rpm in ± 10 minutes. The clear solution obtained was put into a 250 mL separating funnel, then acidified by adding 1 N hydrochloric acid solution to pH 1-2. Furthermore, it was extracted three times, each extraction with 50 mL of ether. Then the ether extract that had been collected was evaporated above a water bath at a temperature of 60-70˚C or evaporated with a vacuum rotary evaporator at a temperature of 55˚C until dry. The obtained extract was dissolved with 5.0 mL methanol and filtered if necessary and put into a vial. Two replications were made (Solution A1 and A2).

Test solution 2, the average weight was determined first for 10 packages/capsules/tablets/liquids and homogenized. Weighed or pipetted an amount of 1 dose of traditional medicine/health supplement and put into a 50 mL centrifuge tube, added 50 mL of mineral-free water, acidified with 1 N hydrochloric acid solution to pH 1-2, then shaken for 30 minutes. The solution was filtered or centrifuged until a precipitate and clear solution were obtained at a speed of 3500 rpm in ± 10 minutes. The clear solution obtained was put into a 250 mL separating funnel, then basetened by adding 1 N sodium hydroxide solution to pH 11-12. Furthermore, it was extracted three times, each extraction with 50 mL of ether. Then the ether extract that has been collected is evaporated above a water bath at

a temperature of 60-70˚C or evaporated with a rotary vacuum evaporator at a temperature of 55˚C until dry. The extract obtained is dissolved with 5.0 mL of methanol and filtered if necessary and put into a vial. Two replications are made (Solution B1 and B2). Mixed test solution: Dipepet Solution A1 and B1 each amounting to 500 µL and put into a GC vial (Solution AB1). Dipepet Solution A2 and B2 each amounting to 500 µL and put into a GC vial (Solution AB2).

### *2.2 Preparation of standard solution and preparation of spiked sample solution*

Master standard solution: Weigh carefully 5 mg each for paracetamol, prednisone, and prednisolone standards and put into the same 5 mL volumetric flask, then add 2 mL of methanol, sonicate until dissolved and then dilute to the limit mark. Working standard solution: Pipette 500 µL of the master standard solution and put into a 5 mL volumetric flask and dilute with methanol to the limit mark. Spiked sample solution 1: The average weight was determined first on 10 packs/capsules/tablets/liquids and homogenized. Weighed or pipetted an amount of 1 dose of traditional medicine/health supplement and put into a 50 mL centrifuge tube, added 5 mg each of standard paracetamol, prednisone, and prednisolone, then added 50 mL of mineral-free water, base with 1 N sodium hydroxide solution to pH 10-11, then shaken for 30 minutes. The solution was filtered or centrifuged at 3000 rpm for 15 minutes. The filtrate obtained was put into a 250 mL separating funnel, then acidified by adding 1 N hydrochloric acid solution to pH 1-2. Furthermore, extracted three times, each extraction with 50 mL of ether. Then the ether extract that has been collected is evaporated above a water bath at a temperature of 60-70˚C or evaporated with a rotary vacuum evaporator at a temperature of 55˚C until dry. The extract obtained is dissolved with 5.0 mL of methanol and filtered if necessary and put into a vial (Solution C).

Spiked sample solution 2: The average weight is determined first for 10 packages/capsules/tablets/liquids and homogenized. Weighed or pipetted an amount of 1 dose of traditional medicine/health supplement and put into a 50 mL centrifuge tube, added 5 mg each of standard paracetamol, prednisone, and prednisolone, then added 50 mL of mineral-free water, acidified with 1 N hydrochloric acid solution to pH 1-2, then shaken for 30 minutes. The solution is filtered or centrifuged at a speed of 3000 rpm for 15 minutes. The filtrate obtained was put into a 250 mL separating funnel, then alkalized by adding 1 N sodium hydroxide solution to pH 11-12. Furthermore, it was extracted three times, each extraction with 50 mL of ether. Then the ether extract that had been collected was evaporated above a water bath at a temperature of 60-70˚C or evaporated with a rotary vacuum evaporator at a temperature of 55˚C until dry. The extract obtained was dissolved with 5.0 mL of methanol and filtered if necessary and put into a vial (Solution D). Mixed sample spike solution: Pipette 250 µL of solutions C and D each and put into a 5 mL volumetric flask and diluted with ethyl acetate to the limit mark (Solution CD).

## 3. Result and Discussion

### *3.1 Traditional medicine*

According to the Indonesian Minister of Health Regulation No. 246/Menkes/Per/v/1990 Traditional Medicine is a material or concoction of materials in the form of plant materials, animal materials, mineral materials, galenic preparations or a mixture of these materials, which have traditionally been used as a treatment based on experience. Traditional medicine is available in various forms, both in ready-to-drink preparations or applied to the skin surface. However, it is currently not available in the form of injections or aerosols. In the form of drug preparations, traditional medicine is available in the form of powder, capsules, tablets, solutions or pills. Based on previous research, it is known that several methods of providing traditional medicine by the Javanese people are, namely by being injected, force-fed, drunk, param-kan, fertilized, and taped (Mulyani et al., 2016). Based on the Decree of the Head of the Food and Drug Supervisory Agency of the

Republic of Indonesia, Number: HK.00.05.2411 concerning the Main Provisions for the Grouping and Labeling of Indonesian Natural Medicines, traditional medicine is divided into 3 categories.

Jamu is a traditional Indonesian medicine based on empirical data and does not require scientific proof up to clinical. However, it must meet the safety criteria according to the requirements that have been set, its efficacy has been proven based on empirical data and must meet the applicable quality requirements (Purwono et al., 2023). Jamu generally consists of 5-50 medicinal plants in powder, pills, drinks or liquids from several plants. For example: Jamu Nyonya Mener, Antangin and Kuku Bima Gingseng (Rahayuda, 2016). Standardized Herbal Medicine (OHT) is a traditional medicine that has been proven to be efficacious and safe pre-clinically (on experimental animals) and has passed acute and chronic toxicity tests. OHT is made from standardized ingredients such as extracts that meet quality parameters and are made hygienically. For example: Tolak angina, Diapet, Fitolac and Lelap (Rahayuda, 2016). Phytopharmaca is a traditional medicine that has been tested for efficacy through pre-clinical tests (on experimental animals) and clinical tests (on humans) and its safety has been proven through toxicity tests. Preclinical tests themselves include several tests, namely: efficacy and toxicity tests, pharmaceutical technology tests to determine the identity or standardized raw materials. Phytopharmaca are produced hygienically, with quality according to established standards. Examples: Stimuno, Tensigard, Rheumaneer, X-gra and Nodiar (Satria, 2013).

### *3.2 Health supplements*

According to Gunawan (1999), supplements are additional substances, not substitutes for nutrients or drugs, because no supplement can replace the efficacy and authenticity of nutrients derived from natural foods. Supplements can be classified into two, namely natural supplements which are the result of extraction from food sources containing natural elements derived from animal and/or plant tissue and synthetic supplements which are generally chemical engineering in the laboratory (Bommakanti et al., 2023). Food supplements are products used to supplement the nutritional needs of food, containing one or more ingredients in the form of vitamins, minerals, amino acids or other ingredients (derived from plants or non-plants) that have nutritional value and/or physiological effects in concentrated amounts. Supplements can be in the form of solid products including tablets, lozenges, effervescent tablets, chewable tablets, powders, capsules, soft capsules, granules, pastilles, or liquid products in the form of drops, syrups, or solutions (Istiany and Rusilanti, 2013). Based on the Regulation of the Food and Drug Supervisory Agency Number 19 of 2022, Health Supplements are products intended to supplement nutritional needs, maintain, improve and/or repair health functions, have nutritional value and/or physiological effects, contain one or more ingredients in the form of vitamins, minerals, amino acids, and/or other non-plant ingredients that can be combined with plants.

According to Atmatsier (2009), there are several types of supplements circulating in the community. Classification of food supplements based on their function. Metabolite drugs to inhibit appetite (*anorexigenicum*): *Anorexigenicum* has the function of inhibiting appetite so that it is often claimed to be able to reduce a person's weight. Drugs to reduce fat and cholesterol (*antilipidemicum*): Antilipidemicum functions to reduce fat and cholesterol, this food supplement is often used to prevent diseases that arise due to high levels of fat and cholesterol in the body. Drugs to improve nutritional status (dietary): Dietaryum has the function of improving nutritional status, dietary food supplements are often used to gain weight or to increase appetite. Energy and spirit boosters: Energy and spirit booster food supplements generally contain vitamins, minerals and herbal extracts such as ginseng and ginger. Medicines to improve the metabolic system of certain organs: Food supplements that function to improve the metabolic system of certain organs include helping with carbohydrate metabolism, fat, collagen structure formation and others. In general, food supplements contain iodine, copper, manganese, zinc and others.

*3.3 Paracetamol, prednisone, and prednisolone*

Paracetamol or acetaminophen, N-acetyl-4 Aminophenol (C8H9NO2), with BM 151.16 and contains not less than 98.0% and not more than 101.0% C8H9NO2. White crystalline powder, odorless and bitter taste. Solubility in 70 parts of water and 7 parts of ethanol (95%) P in 13 parts of acetone P, in 40 parts of glycerol P and in 9 parts of propylene glycol P, soluble in alkali hydroxide solution. Efficacy and uses are analgesic, antipyretic (Katzung, 2011).

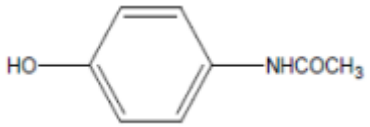


Fig 3. Chemical structure of paracetamol
(Katzung, 2011)

Paracetamol absorption is fast and complete through the digestive tract. The highest concentration in plasma is achieved within 0.5 hours and t1/2 plasma is between 1-3 hours. As much as 25% of paracetamol is bound to plasma proteins, and excreted through the kidneys (Katzung, 2011). The presence of food in the stomach can slow down the absorption of paracetamol preparations so that absorption becomes slow (Katzung, 2011). Paracetamol in the form of a single preparation or containing pure Paracetamol, in the form of tablets or caplets of 500 mg. The usual dose of Paracetamol for adults is 300mg - 1g each time, with a maximum dose of 4 grams per day. In one day, for adults, the dose is given a maximum of 6 times a day (Wilmana & Gan, 2011).

Nonsteroidal anti-inflammatory drugs (NSAIDs) have similar side effects because they are based on inhibition of the prostaglandin biosynthesis system. In general, NSAIDs can cause side effects on three organ systems, namely the digestive tract, kidneys and liver (Katzung, 2011). There are two mechanisms of gastric irritation, local irritation causes diffusion of gastric acid to the mucosa and causes tissue damage and systemic irritation will release PGE2 and PGI2 which will inhibit gastric acid secretion and stimulate small intestine mucus secretion. In some people, hypersensitivity can occur. However, in paracetamol, the side effects are not so dangerous, but if used for a long period of time it can cause liver damage (Goodman & Gilman, 2012).

Prednisone is a compound that in the liver will be immediately converted into prednisolone, an active steroid compound. Steroid compounds are compounds that have a certain chemical structure that has three cyclohexane rings and one cyclopentane ring (Waller et al., 2016). A steroid molecule that is naturally produced by the body's adrenal cortex is known as a corticosteroid compound (Ikawati, 2006). Prednisone has a molecular formula of C21H26O5 with a molecular weight of 358.43 (Departemen Kesehatan RI, 1995).

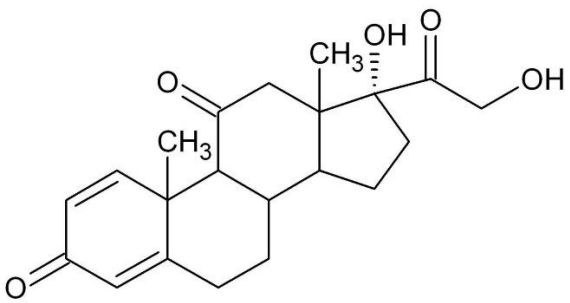


Fig 4. Chemical structure of prednisone
(Departemen Kesehatan RI, 1995)

Prednisone is a synthetic corticosteroid that is generally consumed orally and can also be injected intramuscularly, intrarectally and also topically such as for eye drops or ear

drops and is used to prevent the release of mediators from the body that can cause inflammation. Prednisone is effectively used as an immunosuppressant and can affect the body's immune system. So it can be given to autoimmune diseases, inflammatory diseases (asthma, severe allergies, rheumatoid arthritis, and so on), uveitis and to prevent rejection reactions in organ transplants (Yasir et al., 2025). Prednisone has side effects that are divided into short-term effects and long-term effects. Short-term side effects that can occur from the use of prednisone that is not in accordance with the dose such as increased blood glucose levels especially in patients with diabetes mellitus, fluid retention, insomnia, and euphoria. Long-term effects include Cushing's syndrome, steroid-induced osteoporosis, glaucoma, type 2 diabetes mellitus, migraines, abdominal pain, and weight gain (Yasir et al., 2025). Prednisolone is a steroid drug used to treat certain types of allergies, inflammatory conditions, autoimmune disorders, and cancer. Some of a these conditions include adrenocortical insufficiency, high blood calcium, rheumatoid arthritis, dermatitis, eye inflammation, asthma, and multiple sclerosis. This drug is a used orally, intravenously, as a skin cream, and as eye drops (Darmansjah, 2005).

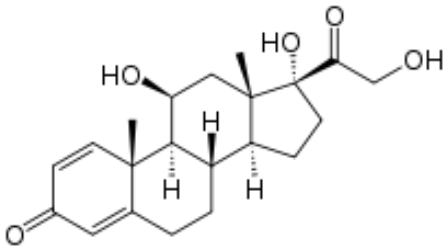


Fig 5. Chemical structure of prednisolone
(Darmansjah, 2005)

Prednisolone is a corticosteroid drug with dominant glucocorticoid activity and low mineralocorticoid activity, making it useful for the treatment of various inflammatory and autoimmune conditions such as asthma, uveitis, rheumatoid arthritis, ulcerative colitis, pericarditis, temporal arteritis and Crohn's disease, Bell's palsy, multiple sclerosis, cluster headache, vasculitis, acute lymphoblastic leukemia, and autoimmune hepatitis, systemic lupus erythematosus, Kawasaki disease, dermatomyositis, and sarcoidosis (Kim et al., 2016). The side effects of prednisolone use are divided into two, namely short-term and long-term. Side effects in short-term use such as nausea and fatigue. More severe side effects such as psychiatric problems, which may occur in about 5% of people who use it (Min et al., 2012). Common side effects in long-term use include osteoporosis, fatigue, fungal infections, and bruising. Although this drug is safe for use in late pregnancy in the short term, it is quite risky for use in early pregnancy with long-term use. This drug is a glucocorticoid made from hydrocortisone (cortisol) (Herretes et al., 2014).

### *3.4 Gas chromathography–mass spectrometer (GC-MS)*

Gas chromatography (GC) is a separation method used to analyze volatile compounds or compounds that are easily evaporated. Compounds that are easily degraded by heat cannot be analyzed by this method. Mass Spectrometer (MS) is an instrumental analysis method used to identify and determine the structure of sample components by showing the relative mass of the component molecules and the relative mass of their fractions (Gandjar & Rohman, 2007).

The working mechanism of GC is that the sample in the form of a mixture to be separated is injected into the injector. Then the sample is carried by the carrier gas into the column. In the column, the components of the sample are separated. The components that have been separated will leave the column and be detected by the detector. Then recorded by the recorder and produce a chromatogram consisting of several peaks (Hendayana, 2006). The components of the gas chromatography system consist of: The carrier gas

functions to carry the components of the mixture that have been separated. The gas used must be inert to the sample or stationary phase, pure, and can be stored in a high-pressure tank. The carrier gases commonly used are helium, nitrogen, hydrogen, or a mixture of argon and methane. The sample injection chamber functions to deliver the sample or sample into the carrier gas flow. The injection chamber must be heated separately from the column at a temperature higher than the maximum column temperature of 10-15$^0$C, so that the sample will evaporate immediately after the sample is injected.

Fig 6. Gas chromathography – mass spectrometer
(Gandjar & Rohman, 2007)

The column functions as a place for the separation process of components from the sample, because it contains a stationary phase. There are two columns in GC, namely packed column and capillary column. The packed column stationary phase can only be coated on the support, while the capillary column stationary phase is coated on the column wall or can even be mixed with a small amount of very fine inert support. The detector is an electronic sensor that converts the carrier gas signal and the components in it into an electronic signal. The electronic signal can present a chromatogram in the form of a series of peak areas against time. The peak area of the chromatogram at a certain retention time can be used as qualitative data and the peak area on the chromatogram can be used as quantitative data (Gandjar & Rohman, 2007).

Mass Spectrometer (MS) is an instrumental analysis method used to identify and determine the structure of unknown sample components by showing the relative mass of the component molecules and the relative mass of their fractions. The use of the mass spectrometry method is intended for: Determination of molecular structure, Proof of stable isotopes in research on biological reactions, Qualitative and quantitative analysis of components that have been isolated and purified (Mulja & Suharman, 1995). GC-MS is a combination of Gas Chromatography and Mass Spectrometer. Mass Spectrometer is connected to the output of gas chromatography. Mass Spectrometer is used as a detector to provide data on the chemical structure of unknown compounds. When the solute gas enters the mass spectrometer, the organic molecules will be shot with high-powered electrons and broken into smaller molecules. Then the components of the mixture that have been separated by gas chromatography will be depicted in one mass spectrum (Hendayana, 2006; Gandjar & Rohman, 2007).

### *3.5 Identification of paracetamol, prednisone, and prednisolone in traditional medicines and health supplements at the Denpasar regional food and drug authority*

#### *3.5.1 Sample preparation and instrumentation*

Paracetamol, Prednisone, and Prednisolone are compounds that are often used in traditional medicines and health supplements. The use of these three compounds can be misused so that their use exceeds the specified limits. So it is necessary to identify the three compounds. This test was carried out on sample 0014 which aims to identify Paracetamol,

Prednisone, and Prednisolone. The method used is in accordance with 103 / OTSK / MA-PPPOMN / 20, namely the method of identifying Paracetamol, Prednisone, and Prednisolone in traditional medicines and health supplements is carried out by Gas Chromatography - Mass Spectrometry (GC-MS). Gas chromatography (GC) is a separation method used to analyze volatile compounds or compounds that are easily evaporated. Compounds that are easily degraded by heat cannot be analyzed by this method. Mass Spectrometer (MS) is an instrumental analysis method used to identify and determine the structure of sample components by showing the relative mass of the component molecules and the relative mass of their fractions. The optimum condition of the tool used in this identification is to use a set of gas chromatography tools equipped with a capillary column containing 5% Diphenyl / 95% Dimethylpolysiloxan (0.25 mm × 30 m, 0.25 μm), and a Mass Spectro detector, sonicator, vortex, centrifuge, centrifuge tube.

A system suitability test was carried out which aims to guarantee the quality of the test results to ensure that the instrument used has good performance. The system suitability test was carried out by injecting 6 times the working standard solution. The %RSD requirement for the system suitability test for this time was 5.3%. %RSD for Paracetamol at retention time and area were 0.030% and 2.842% respectively. For Prednisone, the %RSD for retention time and area were 0.018% and 4.347% respectively, and the %RSD for Prednisolone at retention time and area were 0.017% and 1.586% respectively. In accordance with the requirements of the system suitability test this time, it can be stated that the performance of the Gas Chromatography - Mass Spectrometry used is categorized as good (<5.3%).

### *3.6 Sample and standard preparation*

#### *3.6.1 Preparation of test solutions*

To prepare the test solutions, the average weight of ten capsules, tablets, or liquid sachets of traditional medicine or health supplements was first determined and homogenized. A single dose was then accurately weighed or pipetted into a 50 mL centrifuge tube, followed by the addition of 50 mL of demineralized water. For Test Solution 1, the sample was alkalized with 1 N sodium hydroxide to a pH of 10 to 11 and shaken for 30 minutes. The mixture was centrifuged at 3500 rpm for approximately 10 minutes until clear and sedimented phases were obtained. The supernatant was transferred to a 250 mL separating funnel and acidified with 1 N hydrochloric acid until reaching a pH of 1 to 2. The solution was extracted three times with 50 mL of diethyl ether, and the combined ether extracts were evaporated on a water bath at 60 to 70 degrees Celsius or under reduced pressure at 55 degrees Celsius until dry. The resulting residue was dissolved in 5.0 mL of methanol, filtered if necessary, and transferred into a vial. Two replicates were prepared and labeled as Solution A1 and A2.

Test Solution 2 followed the same procedure with reversed pH treatment. The sample was first acidified with 1 N hydrochloric acid to a pH of 1 to 2 before shaking. After centrifugation, the supernatant was alkalized with 1 N sodium hydroxide until a pH of 11 to 12 was reached, followed by similar extraction and evaporation steps as above. The final residue was also dissolved in 5.0 mL of methanol, filtered if needed, and transferred into a vial. Two replicates were labeled as Solution B1 and B2. Mixed test solutions were prepared by combining 500 μL of A1 and B1 into a single vial (Solution AB1), and another mixed solution was prepared by combining 500 μL of A2 and B2 (Solution AB2).

#### *3.6.2. Preparation of standard and spiked solutions*

To prepare the mixed stock standard solution, exactly 5 mg each of paracetamol, prednisone, and prednisolone reference standards were weighed and dissolved in 2 mL of methanol in a 5 mL volumetric flask. The mixture was sonicated until fully dissolved and diluted to volume with methanol. From this stock solution, 500 μL was pipetted and diluted

to 5 mL to prepare the working standard solution. For spiked sample preparation, the procedure mirrored that of the test solutions, with the addition of 5 mg each of paracetamol, prednisone, and prednisolone into the sample before extraction. In Spiked Sample 1, the sample was alkalized to pH 10 to 11, shaken, centrifuged, acidified to pH 1 to 2, and extracted with ether. In Spiked Sample 2, the sample was acidified first, followed by alkalization after centrifugation. Both extracts were evaporated and redissolved in 5.0 mL of methanol. The two resulting solutions were labeled as Solution C and D, respectively. A mixed spiked sample solution was prepared by combining 250 µL each of Solution C and D into a 5 mL volumetric flask and diluting to volume with ethyl acetate to obtain Solution CD.

### *3.6.3 Compound identification*

Identification of paracetamol, prednisone, and prednisolone was performed using Gas Chromatography–Mass Spectrometry (GC-MS). Each of the test solutions, spiked samples, single standards, mixed standards, and solvent blank was injected individually. The analysis was conducted under the following conditions: helium was used as the carrier gas at a column flow rate of 1.0 mL per minute.

Table 1. Rate of temperature increase

| Rate | Value | Hold Time |
|---|---|---|
| Initial | 100°C | - |
| 25°C/minute | 180°C | 10 minutes |
| 10°C/minute | 280°C | 10 minutes |
| Total analysis time 33.2 minutes | | |

The injection was performed in split mode with a split ratio of 5. The inlet temperature was set to 250 degrees Celsius and the detector at 280 degrees Celsius. The column used was a capillary type containing 5 percent diphenyl and 95 percent dimethylpolysiloxane, measuring 0.25 mm in diameter, 30 meters in length, and 0.25 µm film thickness (e.g., HP-5MS). The ion source was maintained at 230 degrees Celsius with a scan range from 50 to 400 Da. The injection volume was 1 µL, and the temperature program followed the official analytical method 103/OTSK/MA-PPPOMN/20

Table 2. m/z values for SIM mode

| Name | Quantifier | Qualifier 1 | Qualifier 2 |
|---|---|---|---|
| Parasetamol | 109 | 151 | 80 |
| Prednison | 91 | 160 | 121 |
| Prednisolon | 122 | 91 | 147 |

### *3.6.4 Interpretation of results*

The test results were interpreted based on a comparison between the sample solution and both the spiked sample solution and the reference standard solution. A positive identification was confirmed when the sample solution produced a retention time (t) that matched the peak observed in both the spiked sample and the standard solution under the same chromatographic conditions.

Table 3. Ion Mass to Ion Charge Ratio (m/z)

| Relative intensity of qualifier ion(s) compared to target ion | GC-EI-MS (relative deviation) |
|---|---|
| > 50% | ± 10% |
| > 20% to 50% | ± 15% |
| > 10% to 20% | ± 20% |
| ≤ 10% | ± 50% |

The presence of paracetamol, prednisone, or prednisolone was verified by this alignment in retention behavior. In addition to retention time, the identity of the analyte was further supported by comparing the mass-to-charge ratio (m/z) values. A positive result was determined if the sample solution showed the same m/z values and ion intensity ratios as those observed in both the spiked and standard solutions. The consistency in these spectral features ensured that the detected compounds corresponded accurately to the target analytes based on both chromatographic and mass spectrometric data.

### *3.7 Results and discussion*

Paracetamol, prednisone, and prednisolone are compounds commonly found in traditional medicines and health supplements. Due to their pharmacological activity, these substances are prone to misuse, potentially resulting in usage that exceeds the recommended limits (Tiwari et al., 2025). Therefore, it is essential to conduct proper identification of these compounds. In this study, sample 0014 was analyzed with the aim of detecting the presence of paracetamol, prednisone, and prednisolone. The analytical method employed followed the guidelines outlined in 103/OTSK/MA-PPPOMN/20, which describe the procedure for identifying these three substances in traditional medicines and supplements using Gas Chromatography–Mass Spectrometry (GC-MS). Gas Chromatography (GC) is a separation technique used to analyze volatile or easily vaporized compounds. It is not suitable for thermally labile substances that may degrade under high temperatures. Meanwhile, Mass Spectrometry (MS) is an instrumental analytical technique used for identifying and determining the structural characteristics of sample components by measuring the relative mass of molecular ions and their fragments. The instrumentation used in this analysis was optimized under specific conditions, involving a gas chromatograph system equipped with a capillary column containing 5% diphenyl/95% dimethylpolysiloxane (0.25 mm × 30 m, 0.25 µm) and a mass spectrometer detector. Additional tools included a sonicator, vortex mixer, centrifuge, and centrifuge tubes.

A system suitability test (SST) was performed as part of the quality assurance process to ensure that the instrument was functioning properly. The SST was conducted by injecting the working standard solution six times. The relative standard deviation (%RSD) acceptance criterion for this test was 5.3%. The %RSD values for paracetamol were 0.030% for retention time and 2.842% for peak area. For prednisone, the values were 0.018% for retention time and 4.347% for peak area. Lastly, prednisolone showed %RSD values of 0.017% for retention time and 1.586% for peak area. As all %RSD values fell within the acceptable range (<5.3%), the performance of the GC-MS instrument was deemed satisfactory for this analysis.

#### *3.7.1 Results of standard and sample testing*

In identifying Paracetamol, Prednisone, and Prednisolone, testing was first conducted on the standard, with each standard being repeated seven times. The results of the standard testing on Paracetamol, Prednisone, and Prednisolone are as follows:

Table 4. Results of standard and sample testing

| Paracetamol Standard Data | | | | | | | |
|---|---|---|---|---|---|---|---|
| Sample ID | Sample Name | Ret. Time (min.) | Area | Height | Resolution | Tailing Factor | HETP |
| UKS 1 | UKS 1 | 9.608 | 361523 | 51643 | - | 0.892 | 0.000 |
| UKS 2 | UKS 2 | 9.613 | 346386 | 51421 | - | 0.947 | 0.000 |
| UKS 3 | UKS 3 | 9.611 | 348809 | 50399 | - | 0.929 | 0.000 |
| UKS 4 | UKS 4 | 9.607 | 344318 | 51012 | - | 0.967 | 0.000 |
| UKS 6 | UKS 6 | 9.614 | 334164 | 48996 | - | 0.925 | 0.000 |
| UKS 7 | UKS 7 | 9.608 | 336363 | 52732 | - | 0.935 | 0.000 |
| %RSD | | 0.030 | 2.842 | 2.473 | 0.000 | 2.677 | 0.000 |
| Prednisone Standard Data | | | | | | | |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| UKS 1 | UKS 1 | 28.322 | 28062 | 5253 | 1.983 | 1.099 | 0.000 |
| UKS 2 | UKS 2 | 28.331 | 25527 | 5001 | - | 1.014 | 0.000 |
| UKS 3 | UKS 3 | 28.329 | 27438 | 5021 | - | 1.176 | 0.000 |
| UKS 4 | UKS 4 | 28.323 | 25255 | 4684 | 1.581 | 1.340 | 0.000 |
| UKS 6 | UKS 6 | 28.327 | 27677 | 5011 | 1.592 | 1.150 | 0.000 |
| UKS 7 | UKS 7 | 28.336 | 26941 | 5121 | - | 1.066 | 0.000 |
| %RSD | | 0.018 | 4.347 | 3.759 | 81.178 | 9.950 | 0.000 |
| Prednisolone Standard Data | | | | | | | |
| UKS 1 | UKS 1 | 31.354 | 98418 | 13364 | 1.782 | 1.056 | 0.000 |
| UKS 2 | UKS 2 | 31.364 | 94941 | 13710 | 1.997 | 1.022 | 0.000 |
| UKS 3 | UKS 3 | 31.361 | 96027 | 13015 | 1.727 | 1.294 | 0.000 |
| UKS 4 | UKS 4 | 31.358 | 96179 | 14750 | - | 1.075 | 0.000 |
| UKS 6 | UKS 6 | 31.353 | 93923 | 13459 | 2.625 | 1.217 | 0.000 |
| UKS 7 | UKS 7 | 31.350 | 96524 | 13523 | 1.310 | 1.216 | 0.000 |
| %RSD | | 0.017 | 1.586 | 4.339 | 56.109 | 9.582 | 0.000 |

After testing the standards, the identification of Paracetamol, Prednisone, and Prednisolone was continued with testing of the samples, with each sample being tested twice. The results of the standard testing for Paracetamol, Prednisone, and Prednisolone are as follows:

Table 5. Testing standards of paracetamol, prednisone, and prednisolone

| GC Results Data for Sample 0014 for Paracetamol | | | | | | | |
|---|---|---|---|---|---|---|---|
| Sample Name | Sample Amount | Ret. Time (min.) | Area | Height | Resolution | Tailing Factor | HETP |
| 0014 A | 1.000000 | 9.559 | 169 | 77 | - | - | - |
| 0014 B | 1.000000 | - | - | - | - | - | - |
| Sp 0014 MeOH | 1.000000 | 9.546 | 119872 | 20791 | - | 1.184 | 1.184 |
| GC Data Results for Sample 0014 for Prednisone | | | | | | | |
| 0014 A | 1.000000 | - | - | - | - | - | - |
| 0014 B | 1.000000 | - | - | - | - | - | - |
| Sp 0014 MeOH | 1.000000 | 28.316 | 10551 | 1999 | 1.712 | - | 0.000 |
| GC Data Results for Sample 0014 for Prednisolone | | | | | | | |
| 0014 A | 1.000000 | - | - | - | - | - | - |
| 0014 B | 1.000000 | - | - | - | - | - | - |
| Sp 0014 MeOH | 1.000000 | 31.333 | 35157 | 5216 | 1.351 | 1.050 | 0.000 |

After testing the standard and samples to identify Paracetamol, Prednisone, and Prednisolone, the Mass Spectrometer results were broken down into ions called daughter ions (fragmentation). The following is the data from the daughter ions (fragmentation):

Table 6. Standard MS data for Paracetamol

| Standard MS Data for Paracetamol | | |
|---|---|---|
| UKS | m/z | |
| Baku | 80 | 151 |
| 1 | 29.03 | 26.03 |
| 2 | 29.34 | 27.39 |
| 3 | 31.26 | 28.73 |
| 4 | 28.21 | 27.16 |
| 6 | 29.71 | 26.79 |
| 7 | 29.24 | 27.66 |
| Average | 29.47 | 27.29 |
| Standard MS Data for Prednisone | | |
| Baku | 160 | 121 |
| 1 | 61.13 | 57.25 |
| 2 | 62.56 | 56.57 |
| 3 | 69.89 | 53.45 |
| 4 | 65.38 | 60.81 |
| 6 | 64.89 | 52.46 |

| | | |
|---|---|---|
| Average | 62.54 | 55.99 |
| Results of Standard MS Prednisolone | | |
| Baku | 121 | 91 |
| 1 | 42.98 | 25.02 |
| 2 | 36.98 | 29.42 |
| 3 | 37.47 | 26.32 |
| 4 | 37.25 | 26.38 |
| 6 | 36.50 | 26.99 |
| 7 | 37.65 | 28.70 |
| Average | 38.14 | 27.14 |

*3.7.2 Analysis of sample test results*

Paracetamol, Prednisone, and Prednisolone were identified by comparing the analysis results with the Gas Chromatography-Mass Spectrometry (GC-MS) instrument between the analyzed standard results. The analysis results for the Paracetamol, Prednisone, and Prednisolone standards can be seen in Tables 1-3, which contain data on retention time, peak area, peak height, resolution, tailing factor, and HETP. For the identification of Paracetamol, a comparison was made between the retention time (Retention Time) obtained from the sample and the retention time of the standard. The retention time for sample 0014A was 9.559, and for sample 0014B, no retention time was detected. When compared with the retention times produced by the 6 Paracetamol standards (9.608; 9.613; 9.611; 9.607; 9.614; and 9. 608, it can be inferred that samples 0014A and 0014B do not contain Paracetamol. The acceptable range values for Paracetamol based on daughter ion (fragmentation) results can be seen in Table 3.13 below:

Table 7. Acceptability range requirements for Paracetamol

| Type | m/z | % Setting | %of Base Peak | EI Relative | Value EI Relative (±) | Acceptability Range |
|---|---|---|---|---|---|---|
| Target | 100 | 100 | | | | |
| Ref. Ion 1 | 80 | 29.02 | >20-50 | ± 15% | 4.35 | 24.67–33.37 |
| Ref. Ion 2 | 151 | 25.95 | >20-50 | ± 15% | 3.89 | 22.06 –29.84 |

The acceptable range for the first ion with m/z 80 is 24.67–33.37, while the acceptable range for the second ion with m/z 151 is 22.06–29.84. These values serve as reference parameters for confirming the presence of paracetamol based on ion fragmentation patterns observed in the mass spectra. Subsequently, the identification of prednisone was carried out by comparing the retention time (RT) obtained from the sample with that of the reference standard. The retention times for the six standard injections of prednisone were recorded as follows: 28.322, 28.331, 28.329, 28.323, 28.327, and 28.336. However, the retention times for samples 0014A and 0014B did not register within the instrument detection range. Therefore, it can be inferred that samples 0014A and 0014B do not contain prednisone. The acceptable retention time range for prednisone based on the daughter ion (fragmentation) analysis is presented in Table 8 below.

Table 8. Acceptability range requirements for Prednisone

| Type | m/z | % Setting | %of Base Peak | EI Relative | Value EI Relative (±) | Acceptability Range |
|---|---|---|---|---|---|---|
| Target | 91 | 100 | | | | |
| Ref. Ion 1 | 160 | 63.98 | >50 | ± 10% | 6.40 | 57.58 – 70.38 |
| Ref. Ion 2 | 121 | 60.48 | >50 | ± 10% | 6.05 | 54.43 – 66.53 |

The identification of prednisolone was conducted by comparing the retention time obtained from the sample with the retention time of the reference standard. The retention times from samples 0014A and 0014B were not detected by the instrument. When compared to the retention times recorded from six injections of prednisolone standard, which were 31.35, 31.36, 31.36, 31.35, 31.35, and 31.35, it can be assumed that samples

0014A and 0014B do not contain prednisolone. The acceptable range values for prednisolone based on the daughter ion or fragmentation results are shown in Table 9.

Table 9. Acceptability range requirements for Prednisone

| Type | m/z | % Setting | %of Base Peak | EI Relative | Value EI Relative (±) | Rentang Keberterimaan |
|---|---|---|---|---|---|---|
| Target | 122 | 100 | | | | |
| Ref. Ion 1 | 121 | 43.80 | >20-50 | ± 15% | 6.57 | 37.23 – 50.37 |
| Ref. Ion 2 | 91 | 24.65 | >20-50 | ± 15% | 3.70 | 20.95 – 28.35 |

## 4. Conclusion

The conclusions that can be obtained from the implementation of the field work practice of identifying paracetamol, prednisone, and prednisolone are: The results of the Paracetamol test on sample 0014A obtained a retention time of 9,599 and a peak area of 169, for sample 0014B it was not detected either in retention time or peak area, where the results were not close to the results obtained in the standard solution of 9,610 for retention time and 345,261 for peak area, so it was concluded that the sample did not a contain Paracetamol. The results of the Prednisone test on samples 0014A and 0014B were not detected either in retention time or peak area, where the results were different from the results obtained in the standard solution of 28,328 for retention time and 26,817 for peak area, so it was concluded that the sample did not contain Prednisone. The results of the Prednisolone test on samples 0014A and 0014B were not detected either in retention time or peak area, where the results were different from the results obtained in the standard solution of 31,357 for retention time and 96002 for peak area, so it was concluded that the sample did not contain Prednisolone. Based on the analysis method (103/OTSK/MA-PPPOMN/20) it states that the determination of the detection limit (LOD) for Paracetamol is 4.32 µg/g (solid preparation) and 2.02 µg/mL (liquid preparation), for Prednisone is 25.18 µg/g (solid preparation) and 11.78 µg/mL (liquid preparation), and Prednisolone is 86, 86 µg/g (solid preparation) and 40.63 µg/mL (liquid preparation).

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