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Medical Ozone for Antihyperuricemia Major Autohemotherapy using DDBD: Standard Dose Production Analysis

Khairunnisa Syahputra[1]; Ervinawati Elyaswanto[1]; Evita Tiara Maharani[1], Eko Yulianto[5]; Siti Susanti[3]; Sumariyah Sumariyah[2,5] Fadhilah Nur Fahada[4]; K. Sofyan Firdausi[2] and Muhammad Nur[3,5*]
[1]Magister of Physics, Physics Department, Diponegoro University, Tembalang Campus, Semarang, Indonesia, 50275
[2]Physics Department, Diponegoro University, Tembalang Campus, Semarang, Indonesia, 50275
[3]Department of Agriculture, Faculty of Animal Husbandry and Agriculture, Diponegoro University, Tembalang Campus, Semarang, Indonesia, 50275
[4]Regional General Hospital (RSUD) K.R.M.T. Wongsonegoro, Semarang Indonesia 50276
[5]Center for Plasma Research, Diponegoro University, Integrated laboratory, Tembalang Campus, Semarang Indonesia, 50275

Correspondence Author:- Muhammad Nur[3,5*]

Abstract:- Major autohemotherapy is a medical ozone therapy technique that is gaining increasing importance in treating several diseases. Analysis of the production of standard doses of medical ozone for antihyperuricemia in major autohemotherapy using double dielectric barrier discharge (DDBD) with a copper plate electrode configuration has been carried out. The results of the research show that the higher the applied voltage, the greater the concentration obtained for the low flow rate used. From the results above, the dose obtained is between 11.8 µg to 50.7 µg, which is the dose for therapy using the Major Autohrmotherapy method as antihyperuricemia. This dose has been tried on rabbits and the results of the treatment showed antihyperuricemia

Keywords:- *Medical Ozone, Double Dielectric Barrier Discharge, Major Autohemoteraphy (MAH), Hiperurisemia.*

I. INTRODUCTION

Major and minor Ozone autohemotherapy is a medical ozone therapy technique that is gaining increasing importance in treating several diseases [1,2]. For some treatments it has been well validated. Major Auto-Hemotherapy (MAH) involves the injection of medical grade ozone gas into blood taken from a patient. Ozone is mixed with blood. Blood that has undergone ozonation is injected back into the same patient intravenously. Research on MAH is still very necessary. Several studies show that when ozone is injected into a blood sample, it destroys any pathogens. When ozonated blood is injected back into the person, it may have the effect of an autogenous (self-produced) vaccine [1,3]. Furthermore, ozone therapy is gradually being accepted by doctors in various fields. This new treatment using ozone and oxygen was found to be safe, comfortable and cheap [4]. Autohemotherapy is a therapeutic strategy to fight various disorders in animals, especially aiming to improve the immune system with the animal's blood [5]. Autohemotherapy uses a method of injecting a certain amount of blood. This therapy is useful for restoring conditions where immunological balance is disturbed by suppressing abnormal reactions so that the body returns to its original condition with normal sensitivity [6-7].

A very advanced and novel study of this hypothesis was carried out by Díaz-Gómez and Hernández-Rosales, 2023, by analyzing the latest evidence regarding biological ozone formation. This is supported by the concept that reactive oxygen spicies (ROS) generated from the application of parenteral ozone therapy can also cause the formation of endogenous ozone or an oxidant such as ozone [8]. Many studies from several ozone therapy research centers agree that its application is systemic parenteral, ozone therapy mainly produces ROS in the body in the form of hydrogen peroxide and aldehyde compounds. However, under certain conditions, the conversion of these ROS into other ROS having different oxidation powers often occurs [8]. Díaz-Gómez and Hernández-Rosales hypothesized that hypochlorous acid, hydroxyl radicals, and singlet oxygen could be generated from hydrogen peroxide formed by the reaction of ozone with organic biomolecules. Next, the singlet oxygen formed can be a precursor for the formation of endogenous ozone [8]. For medical purposes, the medical ozone generator industry has started in several countries, including Indonesia. Ozone (O_3) is a natural gas compound found in the atmosphere and is formed as a result of UV radiation or high energy [9]. When an oxygen molecule is split into two oxygen atoms, an electrical discharge (spark) occurs which reacts with the oxygen molecule to produce ozone molecules [10]. As an oxidant, ozone has strong antibacterial qualities against bacteria, viruses, protozoa and other microbes. Ozone has several uses, especially in the medical field, due to its qualities, which include wound healing, treatment of skin diseases, and disinfection [11,12,13,].

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When used correctly, ozone therapy can be a powerful therapeutic tool for the human body that does not cause harm and can help in various pathological disorders [14]. The free radicals released when O_3 breaks down act as oxidants [15-16]. The double dielectric barrier discharge (DDBD) reactor is one type of medical reactor that is appropriate because there is a gap between the two barriers that allows pure oxygen to pass through [14,15,16,17]. Small amounts of oxygen or ozone are used as medical ozone [18]. Ozone has the ability to remove germs, viruses, sterilize and kill cancer cells and kill or destroy dangerous bacteria [19]. By adjusting the voltage and gas flow rate, this research uses DDBD with copper plate electrodes to determine its effect on ozone concentration to obtain the dose that will be used in medical ozone therapy using the major autohemotherapy method. Based on the description above, this research will observe the optimal oxygen flowrate to produce ozone concentration using a DDBD reactor with a copper plate configuration. So it can be applied for medical purposes and carry out dosage suitability tests based on the regulations issued by the Madrid Declaration on Ozone Therapy in 2023 for major Autohemotherapy for antihyperuricemia for small animals.

II. RESEARCH METHODS

This research uses DDBD using a copper plate which has a cylindrical shape for as shown in Figure 1. The DDBD reactor has an outer diameter of 4.01 cm, an inner diameter of 1.93 cm, a thickness of the reactor glass of 0.3 cm, a copper plate reactor length of 17 cm, the length of the outer electrode and in 10 cm. A pulsed AC high voltage source with a frequency of 60 Hz (produced by Dipo Technology, Indonesia) and a voltage range of 0.5 kV to 3.4 kV was installed on both electrodes. An ammeter and multimeter (Sanwa YX361TR, China) were also connected to the electrodes to identify current and volatage. To obtain the concentration from the ozone monitor, a hose will be connected from the end of the reactor to the ozone monitor. Ozone produced by the DDBD reactor is measured with an ozone monitor (2B Technologies An InDevR Company 106-M Serial 1182M), China and specifications with specifications for using a maximum flow rate of 1.5 L/Minute and can read ozone concentrations ranging from 0 to 1.000 mg/l). Oxygen gas from medical oxygen tube is regulated through a normalized flow meter for 20^0C air, 1 atm, with a measurement limit of 0.1 L/min - 0.8 L/min, with brand of Wie Brock.

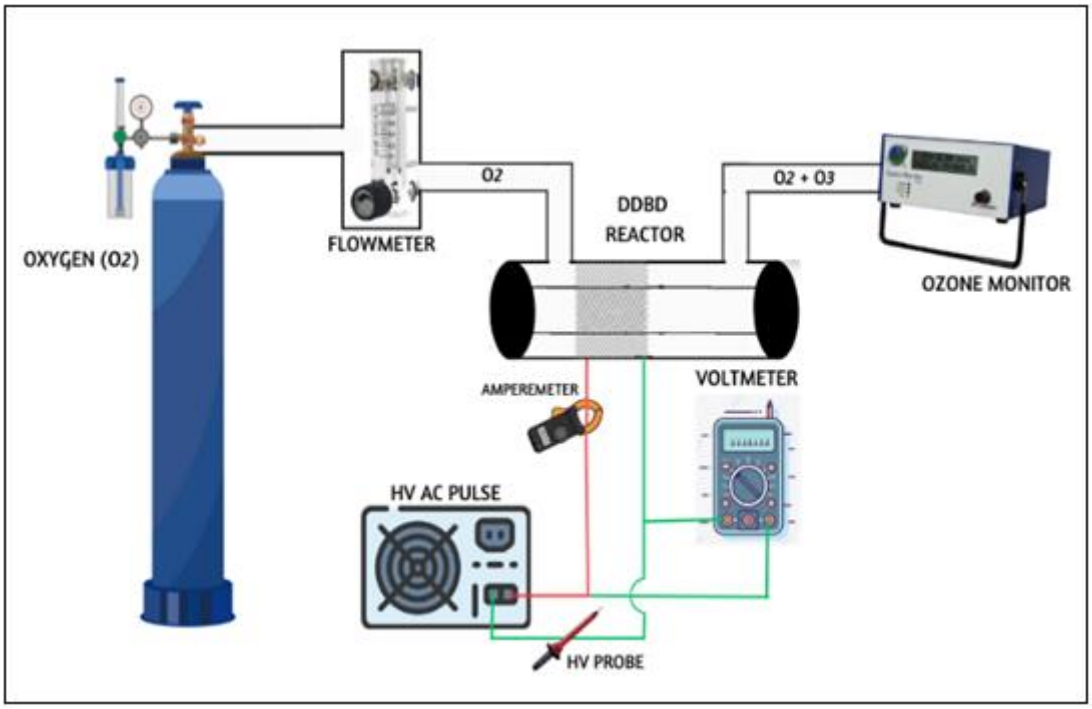

Fig 1 Ozone Generator Setup Scheme

- *The Ozone Concentration is Obtained from the Output Value on the Ozone Monitor by Varying the Voltage, Current and flow rate. Capacity can be Calculated using the Formula:*

- Capacity = C_{ozone} (mg/L) x flowrate (L/min) (1)
- Dosage = Capacity (mg/min) x time (min) (2)

III. RESULT AND DISCUSION

A. Effect of Voltage on Concentration and Capacity

The reactor operating voltage will affect the amount of power used by the reactor. The addition of voltage affects the increase in power which is calculated from multiplying the voltage by the resulting current. At a voltage of 2.8 kV to 3.3 kV there is a fairly rapid increase in power consumption.

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The process of ozone formation begins with the collision of electrons on oxygen molecules. Electrons are released from gas molecules because they are exposed to a high electric field caused by high operating voltage. The initial electrons resulting from the ionization of gas molecules are accelerated by a high intensity electric field. These electrons collide with oxygen atoms in the reactor. This collision results in the multiplication of electrons and produces ions and free radicals. The ions that may be formed are O^+, O_2^+, O_2^-, and O_3. Ions and radicals are very reactive so they react with each other and will produce new species, namely ozone. Ozone formation begins with dissociation (3), dissociative enhancement (4) and dissociative ionization (5) as follows:

- Dissociation $e^- + O_2 \rightarrow 2O^* + e^-$ (3)
- Disiative Engagement $e^- + O_2 \rightarrow O^* + O^-$ (4)
- Disassociative ionization $e^- + O_2 \rightarrow O^* + O^* + 2e^-$ (5)

➢ Oxygen radicals will then react with oxygen to produce ozone (7) with the help of neutral molecules as a catalyst.

- $O_2 + e \rightarrow 2O + e$ (6)
- $O + O_2 + M \rightarrow O_3 + M$ (7)

The ozone concentration increases due to the increased voltage, as in Figure 2 where the electric field in the reactor is formed which becomes higher so that the electrons have high energy to produce electrons whose movement is faster, causing more ionization to dissociation. Many ions will be free and radicals will be formed. This causes the resulting ozone to have a greater concentration. The ozone concentration is also generated through an ozone monitor which has an accuracy of 0.01 µg. Ozone capacity is calculated from multiplying the ozone constant by the flow rate by the linear voltage. The concentration and capacity of ozone increases with increasing voltage. Gambar 3 menujukkan kapasitas ozon sebagai fungsi tegangan operasi untuk beberapa flowrate. Kapasitas ozon yang diperoleh inilah yang telah digunakan untuk mendapatkan dosis yang bersesuaian dengan standard yang telah disepakati dalam deklerasi Madrid [18].

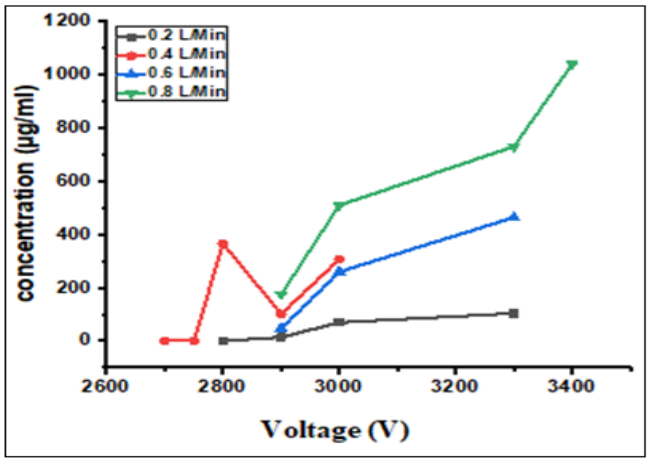

Fig 2 Graph Characteristic Concentration as a Function Voltage

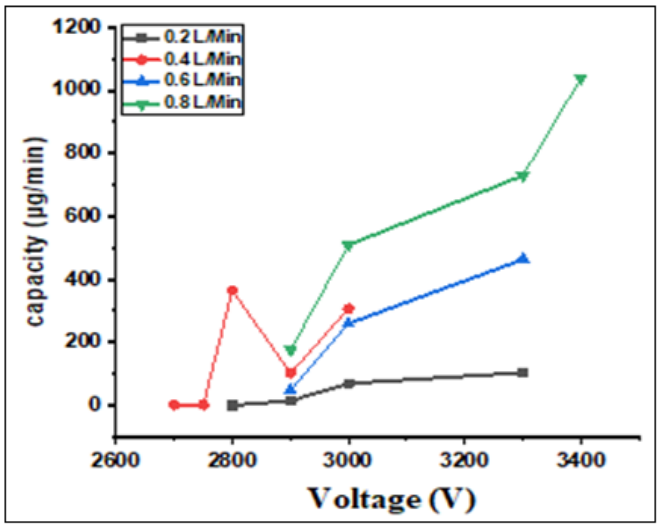

Fig 3 Graph Characteristic Capacity as a Function Voltage

B. Doses and the Application for Medical Therapy

The influence of flowrate variations on concentration values was investigated in this study. At higher voltages and greater flowrates, the reactor produces ozone with higher concentrations, while the voltage is high enough for the ozone formation mechanism to occur. This concentration value is produced by an ozone generator. The length of the reactor affects the ozone concentration. The longer the reactor, the resulting ozone concentration increases. This is caused by the number of oxygen molecules in the plasma zone in the reactor. The longer the reactor, the more molecules there will be in the reactor, so there will be more collisions. The collision of energetic electrons with molecules will result in greater dissociation and ionization compared to shorter reactors, because the plasma zone is shorter.

Medical ozone uses 99.99% pure oxygen gas as its input gas source. Medical ozone generators cannot use mixed oxygen/air, because they contain nitrogen components which allow the formation of nitrogen oxides which are harmful to the human body[18,19]. The application of ozone for therapy has been carried out in treating pathological diseases such as diabetic foot, ischemic syndrome, and other diseases that have undergone testing and validation [4-7] via reduced bacterial infection, or increased oxygen levels after ozone exposure had a healing effect on the wound [8, 9,11,12,22]. The ozone dose results are shown in Figure 4. This figure shows ozone dosage as function of time with operation voltage of 2900 V. The medical use of ozone is supported by the ease with which ozone dissolves in blood or other body fluids. Based on the hypothesis of Díaz-Gómez and Hernández-Rosales that hypochlorous acid, hydroxyl radicals, and singlet oxygen can be produced from hydrogen peroxide formed by the reaction of ozone with organic biomolecules. Biochemical processes occur in biological tissues in the body. The healing process will occur if the appropriate dose has been used in the therapy. In-depth research with clinical trials that meet ethical clearance standards is very necessary for the use of medical ozone.

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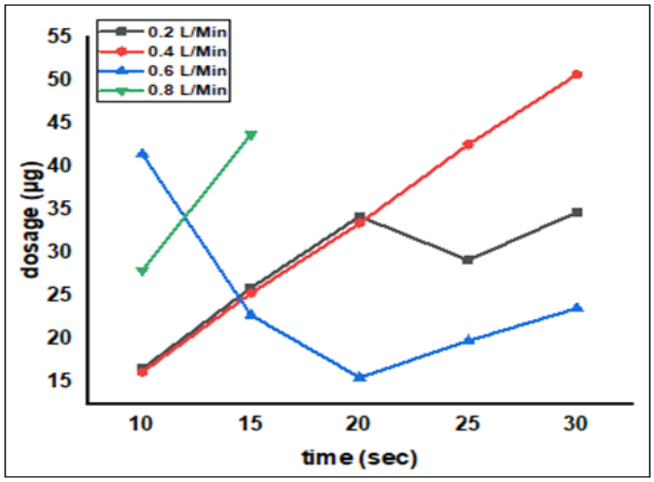

Figure 4. Graph characteristic dosage as a function of time for opeartion voltage of 2900 volt.

What about the unfavorable side effects in medical use of ozone? Ozone will have the same effect or impact throughout the world if used for certain diseases or conditions. Application in the wrong way or dose will cause side effects or ineffectiveness of ozone.

Table 1 Protocol for the application of ozone in veterinary medicine [7] (International Scientific Committee of Ozone Therapy, 2020)

Methods	O_3	Dose			Observation
		High	Medium	Low	
MAH	C. (µg/NmL)	30-35	20-30	10-20	Sampel Volume mL/kg (blood)
	V. (mL/Kg)	1-1.5			
	Dosis (µg/g)	30-35 45-52	20-30 30-45	10-20 15-30	

Therefore, there is a protocol as a standard basis and guideline for the use of medical ozone. One of the guidelines regarding the concentration or dose of ozone needed for therapy or treatment can be seen in Table 1.Below in table 1 shows the dose data that can be applied to several ozone therapies

In this study, 15 seconds with a flow rate of 0.6 L/minute produced an ozone dose of 12 µg as a low dose. In 30 seconds with a flow rate of 0.2 L/minute it produces an ozone dose of 34 µg. So this configuration can be applied as a wound healer and treatment for stage 1 and 2 burns. Based on Table 1, it can be seen that the ozone dose obtained from a flowrate of 0.2 L/min to 0.8 L/min ranges from 16 µg to 50 µg which can be used for application in major autohemotherapy methods for small animals.

IV. CONCLUSION

The DDBD reactor can be used as a reactor that produces medical ozone, where if the voltage is higher with a constant flow rate, the current produced will be higher so that the ozone concentration obtained will also be higher. The correct dose can provide medically beneficial effects, in this case it shows that at a frequency of 60 Hz with a reactor length of 17 cm, an ozone dose in the range of 15 µg to 52 µg is obtained, for all flow rates used, namely 0.2 L/min - 0.8 L/ min. Based on the International Scientific Committee of Ozone Therapy, 2020, this dose value can be applied to systematic autohemotherapy treatment [7,22].

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