

TEST OF STIMULATIVE EFFECTS GENERATED BY SOME DRUGS ON THE SYMPATIC AND PARASYMATIC NERVE SYSTEMS IN TRIED ANIMALS

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ABSTRACT

This study aims to determine the anatomy of nerve cells, especially the autonomic nervous system, and to distinguish the effects of stimulation and inhibition of the sympathetic and parasympathetic nervous systems, which are nervous systems that work under the autonomic nervous system. In experimental animals, mice and mice were given several drugs belonging to the cholinergic drug class in the form of metochlorpramide, pilocaprin and adrenaline which would inhibit or have different effects and activities.

The method used in this study is a laboratory experimental method using 4 experimental animals, namely 3 males and 1 female mice, where each mouse is given drug treatment by injecting intra-peritoneally and orally.

The results obtained showed that after administration of several drugs, namely metoclopramide, pilocarpine and adrenaline, showed that these drugs had an effect on the autonomic nervous system or an effect commonly felt by experimental animals. The effects felt on the autonomic nervous system include tremor, diameter, dieresis, miosis, saliva and vasodilation at different time intervals.

Keywords: the sympathetic nervous system, the sympathetic nervous system

INTRODUCTION

In the world of pharmacy, this autonomic nervous system is very important to study because we can find out the mechanism of action of drugs that will affect the autonomic nervous system, therefore one of the reasons for doing this practicum is to see how the effects of some drugs can affect the autonomic nervous system.

The higher a living thing develops, the greater the level of its needs, in this case including the need for information delivery systems, coordination systems, and regulatory systems, in addition to the need for supply organs and secretory organs.

The brain is a group of nervous systems that are most closely related to regulating their own activities and the activities of one another in dynamic and complex ways. In the brain there is a nervous system that regulates all information into brain memory.

The nervous system is divided into two based on anatomical divisions, the central nervous system (CNS), which consists of the brain and spinal cord, and the peripheral nervous system which consists of nerve cells other than the brain and the spinal cord, namely the nerves that enter and leave the CNS.

The nervous system is a series of complex and continuous organs consisting mainly of nervous tissue. In the

Test of Stimulative Effects Generated by some Drugs on the Sympatic and Parasympatic Nerve Systems in Tried Animals

mechanism of the nervous system, the internal environment and external stimuli are monitored and regulated. Specific abilities such as irritability, or sensitivity to a stimulus, and conductivity or the ability to transmit a response to stimulation. The nervous system or system is one of the smallest parts of the organs in the body, but it is the most complex part. The nervous system has a fast flow of information with a high processing speed and is dependent on electrical activity (nerve impulses).

The autonomic nervous system regulates the unconscious tissues and organs of the body. The tissues and organs that are regulated by the autonomic nervous system are the blood vessels and the heart. The autonomic nervous system is composed of nerve fibers that originate in the brain.

The functions of the sympathetic and parasympathetic nervous systems are always opposite (antagonistic). The two sets of neurons in the autonomic component of the peripheral nervous system are afferent or sensory neurons and efferent or motor neurons. Afferent neurons send impulses to the central nervous system, where the impulses are interpreted. Efferent neurons receive impulses (information) from the brain and pass these impulses through the spinal cord to the cells of the effector organs.

The efferent pathways in the autonomic nervous system are divided into two branches namely the sympathetic nerve and the parasympathetic nerve. Where these two nervous systems work on the same organs but produce the opposite response in order to achieve homeostasis (balance). The action of drugs on the sympathetic nervous system and the parasympathetic nervous system can be either a stimulating or a suppressive response.

The organs of the body are generally innervated by sympathetic and

parasympathetic nerves, which perform a diagnostic function, when one inhibits its function, the other stimulates that function. Another example is the stimulation of the central nervous system which will appear in mice in the form of straub, excessive grooming, mydriasis or dilated pupil of the eye which occurs under the influence of the sympathetic nerves, whereas myosis occurs under the influence of parasympathetic [3].

Almost all control functions of the human body are performed by the nervous system. In general, the nervous system controls rapid body activities such as muscle contractions. Sensitivity and conductivity are the main characteristics of living things in reacting to changes in their surroundings. This stimulation is called the stimulus. The resulting reaction is called a response. Living things that are single-celled (unicellular) and multicellular (multicellular) are determined by their ability to function by the cell protoplasm [8].

The flow of information in the nervous system can be broken down schematically into three stages. An external or internal stimulus that hits the sensory organs will induce the formation of impulses that travel to the central nervous system (CNS) (afferent impulses), a complex processing occurs in the CNS (information processing) and as a result of processing, the CNS forms impulses. which travels in a peripheral direction (efferent impulses) and affects the motor response to the stimulus.

The nervous system consists of nerve cells (neurons) which are arranged to form the pusa nervous system. Nerve cells (neurons) are responsible for the transfer of information to the nervous system and peripheral nervous system. The central nervous system (CNS) is the ability to transmit a response to stimulation, consisting of the brain and spinal cord, while the peripheral (peripheral) nervous

system is a nervous system outside the central nervous system that carries messages to and from the central nervous system [4].

The autonomic nervous system is a nervous system that cannot be controlled by our will through the brain. The autonomic nervous system controls several organs such as the heart, blood vessels, kidneys, pupils, stomach and intestines. This nervous system is triggered (induced) or inhibited (inhibited) by drug compounds [11].

There are three components that must be owned by the nervous system, namely: 1) Receptors, are means of receiving stimuli or impulses. In our body that acts as a receptor are the sense organs; 2) Conducting impulses, carried out by the nerve itself. Nerves are composed of connecting fibers (axons). In the connecting fibers there are special cells that extend and expand. Nerve cells are called neurons; 3) Effector, is the part that responds to stimuli that have been delivered by impulse conductors. The most important effectors in humans are muscles and glands [1].

Based on anatomical and neurotransmitter considerations, SSO is divided into sympathetic and parasympathetic branches. The sympathetic system is normally active continuously and makes adjustments at any time to changes in the environment. The sympathoadrenal system can also be released as a unit, especially in times of anger and fear, and affects sympathetically innervated structures throughout the body simultaneously, increasing heart rate and blood pressure, moving blood flow from the skin to the splanchnics to the skeletal muscles, increasing blood sugar, dilating bronchioles and pupil, and in general preparing the organism for "fight or flight" [2].

When fully activated, the sympathetic nervous system produces a "fight or

flight" response, which prepares the body for a crisis that may require sudden and intense physical activity. This system prepares the body to increase the level of somatic activity. Increased sympathetic activity generally stimulates tissue metabolism and increases alertness. The sympathetic nervous system also tends to engage in mass stimulation whereas the parasympathetic causes a specific local response.

The parasympathetic nervous system has preganglionic neuron cell bodies in the brainstem and sacral segments of the spinal cord. The mesencephalon, pons, and medulla oblongata found in the brain stem have an autonomic nucleus that sends motor commands to the cranial nerves while in the sacral segments the autonomic nucleus resides in the gray horns on S2-S4.

The parasympathetic system is primarily regulated for isolated and localized excretion, slows the heart rate, lowers blood pressure, stimulates movement and secretion of the gastrointestinal tract, assists absorption of nutrients, protects the retina from excess light, and empties the bladder and rectum [2].

The functions of the autonomic nervous system are as follows:

Sympathetic nerve function increases

1. The stimulatory effect of the sympathetic division: the sympathetic effect is to increase heart rhythm and blood pressure, mobilize the body's energy reserves and increase blood flow from the skin and internal organs. Sympathetic stimulation also causes dilatation of the pupils and bronchioles.
2. The "fight or flight" response: these reactions are triggered by direct sympathetic activation of the effector organs and by stimulation of the adrenal medulla to release epinephrine and small amounts of norepinephrine. These hormones enter the bloodstream

Test of Stimulative Effects Generated by some Drugs on the Sympatic and Parasympatic Nerve Systems in Tried Animals

and increase the response of effector organs that have adrenergic receptors [8].

Parasympathetic nervous system functions

The parasympathetic nervous system maintains essential body functions such as the digestion of food and the reduction of waste substances, and these are necessary to sustain life. This system usually acts against and counterbalances sympathetic action and is usually more dominant than the sympathetic system in "rest and digest" situations. The parasympathetic nervous system is not a functional manifestation like the sympathetic system and never copes with it as a complete system. If this system works, it will produce massive, unexpected and unpleasant symptoms. Instead, the separate parasympathetic fibers will be activated separately as well and the system works to affect specific organs such as the stomach and eyes [9].

Receptors are commonly called presynaptic receptors found throughout the central and peripheral nervous system. The term presynaptic receptor denotes the receptors found on the presynaptic side of the synapse. These receptors are felt to provide feedback to the neuron regarding the level of activity at the synapse. Activation or inhibition of these receptors can modulate the release of neurotransmitters from the synapse. In the autonomic nervous system, the presynaptic receptors that get the most attention are the α_2 receptors. Presynaptic activation of the α_2 receptor decreases NE release. essentially, when a certain amount of NE has been released into the synaptic cleft, the presynaptic receptors are activated to reduce the release of more NE [12]. Receptors are protein molecules that are normally activated by transmitters and hormones. There are four main types of receptors as below:

1. Agonist (ligand) -gated channels consist of protein subunits that form a

- central pore (e.g. nicotine receptors, α -aminobutyric acid (GABA) receptors;
2. G-protein coupled receptors (receptors that bind to G proteins) form a receptor group with seven helices that make up the membrane. These receptors are associated (usually) with physiological responses by second messengers;
 3. Core receptors for steroid and thyroid hormones are set up in the cell nucleus and regulate transcription and subsequently protein synthesis;
 4. Kinase-linked receptors are surface receptors that have (usually) intrinsic tyrosine kinase activity. These receptors include insulin receptors, cytokines, and growth factors.

In the autonomic nervous system, two neurons are needed to reach the target organs, namely the praganlionic neurons and the post-tranaglionic neurons. All of the pranglionic neurons release acetylcholine as their transmitter [7].

The differences between the sympathetic and parasympathetic nervous systems have physiological and functional correlations. The sympathetic nervous system has extensive influence throughout the body, whereas the parasympathetic supplies only the visceral structures served by the cranial nerves or those in the abdominopelvic cavity. Although some organs are served by only one SSO division, most organs receive dual innervation, that is, receiving instructions from sympathizers and parasympathizers.

The structure between the sympathetic he ganglion position. The sympathetic nerve has a ganglion which is located along the spine attached to the spinal cord so that it has a short pre-ganglion vein, while the parasympathetic nerve has a long pre-ganglionic vein because the ganglion attaches to the organ.

The sympathetic and parasympathetic nervous systems are always active and their basic activity is regulated by sympathetic tone or parasympathetic tone.

This tonic value causes changes in activity in the organs it supplies both to increase and decrease in activity. For example, the tone of the sympathetic nervous system normally causes only about 50% constriction of the blood vessels. Increased or decreased activity of the sympathetic nervous system causes these changes interconnected in the resistance of the vascular system. In the absence of sympathetic tone, the sympathetic nervous system causes only vasoconstriction.

In addition, as previously explained, coordination between the sympathetic and parasympathetic nervous systems also occurs in the presence of α_2 receptors in the parasympathetic division. When the parasympathetic division is active, NE is released by sympathetic stimulation and then binds to the parasympathetic neuromuscular and neuroglandular junctions thereby inhibiting its activity.

Autonomic nervous system drugs are divided into 5 main parts, namely: Parasympathomimetics or cholinergics. The effects of this class of drugs resemble those arising from the activity of the parasympathetic nervous system. Sympathomimetic or adrenergic effects resembling those caused by sympathetic nervous system activity. Parasympatholytic or cholinergic inhibitors inhibit the effect due to the activity of the parasympathetic nervous system. Sympatholytic or adrenergic inhibitors inhibit the effects of sympathetic nervous activity. Ganglion drugs stimulate or inhibit impulse transmission in the ganglion [5].

Autonomous drugs are drugs that can affect the transmission of impulses in the autonomic nervous system by interfering with the synthesis, storage, release, or breakdown of neurotransmitters or by affecting their action on specific receptors. The result is the influence of smooth muscle function and organs, heart, and dopamine glands [12].

According to the benefits of autonomic medicine, it can be classified as follows:

1. Substances that act against SO namely:
 - a. Sympathomimetics (adrenergics), which mimic the effects and stimulation of SO by, for example, non-adrenaline, ephedrine, isoprenaline and amphetamines;
 - b. Simpatolitika (adrenolitika), which actually suppresses the sympathetic nerves or counteracts the adrenergic effect, for example the alkaloids sekale and propranolol.
2. Substances that work against SP, namely:
 - a. Parasympathomimetics (cholinergics) that stimulate the organs served by the parasympathetic nerve and mimic the stimulating effect with acetylcholine, for example pilocarpine and fisostigmine.
 - b. Parasympatholytics (anticholinergics) that actually counter the effects of parasympathomimetics, for example the alkaloids belladone, propantheline, and mepenzolate.
3. Ganglionic blocking agents, which block the transmission of impulses in sympathetic and parasympathetic ganglionic cells. These inhibiting effects have broad implications, including vasodilation due to blockade of the sympathetic dopamine system [13].

The classification of SSO drugs can also be as follows:

1. Cholinergic antagonist, *cholinergic agonists are divided into 3 groups, namely:*
 - a. Work straight away, the drugs included in this group are: acetylcholine, betanekol, carbakol, and pilocarpine;
 - b. Works indirectly (reversible), the drugs included in this group are: edrophonium, neostigmine, fisostigmine, and pyridostigmine;

Test of Stimulative Effects Generated by some Drugs on the Sympatic and Parasympatic Nerve Systems in Treated Animals

- c. Works indirectly (irreversible), the drugs included in this group are: ecotiofates and isoflurofates.
2. Cholinergic antagonists, *Cholinergic antagonists are divided into 3 groups, namely:*
 - a. Antimuscarinic drugs, the drugs included in this group are: atropine, ipratropium, and scopolamine;
 - b. Ganglionic insulation, the drugs included in this group are: mecamlamine, nicotine, and trimetafan;
 - c. Neuromuscular blockers, the drugs included in this group are: atracurium, doxacurium, metokurine mivacurium, pancuronium, pipercuronium, rocuronium, succinylcholine, tubocurarine, and vecuronium.
3. Adrenergic agonists, *Adrenergic agonists are divided into 3 groups, namely:*
 - a. Work straight away, the drugs included in this group are: albuterol, clonidine, dobutamine, dopamine, epinephrine, isopreterenol, metapreterenol, methoxamine, norepinephrine, phenylephrine, ritodrine and terbutaline;
 - b. Indirect work, the drugs included in this group are: amphetamines and tyramines;
 - c. Double work, the drugs included in this group are: ephedrine and metaraminol.
4. Adrenergic antagonists, *Adrenergic antagonists are divided into 3 groups, namely:*
 - a. Insulator, the drugs included in this group are: doxazosin, phenoxinbenzamine, fentolamine, prazosin, and terazosin.
 - b. Insulator, the drugs included in this group are: acebutolol, atenolol, labetalol, metoprolol, nadolol, pindolol, propranolol, and timolol [6].

Experimental Animal Classification and Habitat

Classification of Mice (*Mus Musculus*):

Kingdom	: Animalia
Phylum	: Chordata
Sub Phylum	: Vertebrates
Class	: Mammals
Sub Class	: Rodentia
Family	: Muridae
Genus	: <i>Mus</i>
Species	: <i>Mus Musculus</i>

RESEARCH METHODS

This research was conducted at the Laboratory of the University of Bina Mandiri Gorontalo. The method used is a laboratory experimental method using 4 experimental animals consisting of 3 male mice and 1 female mouse. Then the mice were weighed and the dose for each drug was calculated based on the calculation of the dose and then converted from human to animal trials. After that, the experimental animals were given pilocarpine and adrenaline by injecting intra-peritoneally and for the drug metoclopramide given orally. After giving the three drugs, observe the symptoms that arise in the experimental animal. Symptoms that can be observed are pupils, diarrhea, dieresis, tremor, ear vein color, saliva, dryness, grooming and exophthalmic.

Tools and materials

The tools used in this study were the syringe, erlenmeyer, beaker, cannula, cotton, and measuring flask. The materials used in this study were adrenaline, metochloropramide, na cmc, pilocarpine, and propranolol.

RESEARCH RESULT

This research was conducted in the laboratory of the University of Bina Mandiri Gorontalo using a sample of 4 experimental animals, namely mice (*Mus musculus*) consisting of 3 male mice and 1 female mouse. Figure 1. below shows

the treatment of *Mus musculus* experimental animals

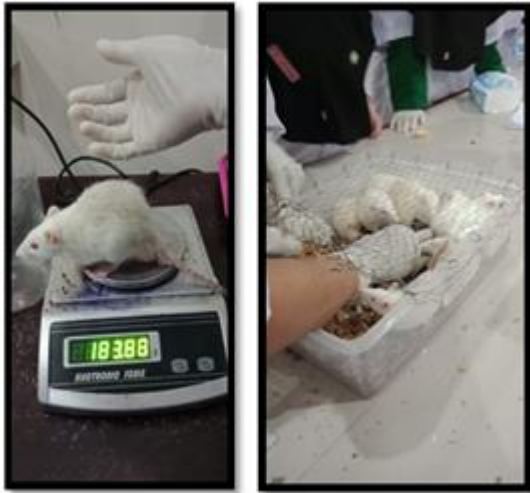


Figure 1. The treatment process

In Figure 1. There are several treatments aimed at experimental animals before administering the drugs, where before giving the drug, mice must be weighed beforehand so that the weight of the mice can be determined. Where this measurement is intended to determine the dose conversion to be given to experimental animals.

Figure 2. below is the process of administering the drug to experimental mice (*Mus musculus*).



Figure 2. The process of drug administration

In Figure 2. There are 2 different treatments at the time of drug administration, where metoclopramide is administered intravenously and pilocarpine and adrenaline are administered intraperitoneally. This difference in administration is due to the different mechanisms of these three drugs,

for pilocarpine and adrenaline given intraperitoneal because these two drugs act by stimulating muscarinic receptors and smooth muscle in the iris and secretion. As for the drug metoclopramide is given orally because this drug works by blocking dopamine receptors and in higher doses this compound can block serotonin receptors in the counter-receptor trigger zone in the central nervous system, as well as accelerate gastric emptying so it can reduce nausea and prevent vomiting [10].

The results showed that there were symptoms arising from the administration of the drug in male and female mice, the results of this study can be presented in the table below.

Male mice

The following table describes the effects of tremor observed for 60 minutes in male mice

Table 1. Metochloropramide (Male)

No.	Effects Observed	Time of Symptoms (Minutes)					
		0-10	10-20	20-30	30-40	40-50	50-60
1	Miosis	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
2	Diara	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
3	Diuresia	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
4	Tremor	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>
5	Vasodilation	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
6	Saliva	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
7	Sweat	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

Table 1 shows the results that the administration of metoclopramide gives a tremor effect. This effect occurs at 10-20, 20-30, 30-40 and 40-50 minutes. Meanwhile, the other effects were not felt by the experimental animals after metoclopramide drug administration.

The following table describes the effects of diuresis and diarrhea observed for 60 minutes in male mice.

Test of Stimulative Effects Generated by some Drugs on the Sympatic and Parasympatic Nerve Systems in Tried Animals

Table 2. Adrenaline (Male)

No	Effects Observed	Time of Symptoms (Minutes)					
		0-10	10-20	20-30	30-40	40-50	50-60
1	Miosis	√	√	√	√	—	—
2	Diaera	—	—	√	—	—	—
3	Diuresia	—	—	√	—	—	—
4	Tremor	—	√	—	—	—	—
5	Vasodilation	√	—	√	—	—	—
6	Saliva	√	—	—	√	—	—

Table 2. shows the results that after administration of adrenaline there were 2 effects felt by the experimental animals, namely the effects of dieresis and diarrhea. These two effects occur simultaneously in the 10-20 minute and 20-30-minute mark. Other effects were not felt by the experimental animals after giving adrenaline.

The following table describes the effects of miosis, diaera, diuresia, tremor, vasodilation, saliva and sweating observed for 60 minutes in male mice.

Table 3. Pilocaprine (Male)

No	Effects Observed	Time of occurrence Symptoms (Minutes)					
		0-10	10-20	20-30	30-40	40-50	50-60
1	Miosis	□	√	□	□	□	□
2	Diaera	√	□	√	√	□	□
3	Diuresia	□	—	√	√	□	□
4	Tremor	□	√	□	□	□	□
5	Vasodilation	√	□	√	□	□	□
6	Saliva	□	√	√	√	□	□
7	Sweat	√	√	√	√	√	√

Table 3. shows the results that after administration of pilocarpine, experimental animals experienced miosis effects that occurred at 10-20 minutes, diaera effects at 0-10, 20-30 and 30-40 minutes, diuresia effects at 20-30 and 30 minutes. -40, the teremor effect at 10-20 minutes, the vasodilating effect at 0-10 and 20-30 minutes, the salivary effect at 10-20, 20-30 and 30-40 minutes and the sweating effect occurs in the 0- 60.

Female mice

Since only one female mice were used, the only treatment carried out was the administration of metochlororamide drugs individually.

Table 4. Pgiving metochlororamide drug individually in female mice

No.	Observed effect	Time of symptom (minutes)					
		0-10	10-20	20-30	30-40	40-50	50-60
1	Miosis	□	□	□	□	□	□
2	Diaera	□	√	√	□	□	□
3	Diuresia	□	√	√	□	□	□
4	Tremor	□	□	□	□	□	□
5	Vasodilation	□	□	□	□	□	□
6	Saliva	□	□	□	□	□	□
7	Sweat	□	□	□	□	□	□

Table 4 shows the results that after administration of the drug metoclopramide in female mice, the effect that occurs is in the form of myosis at 0-40 minutes, diameter effects at 20-30 minutes, the effects of diuresa at 20-30 minutes, tremor effect in 10-20 minutes, vasodilation effect in minutes to 0- 10 and 20-30 and the salivary effect occurs at minutes to 0-10 and 30-40.

DISCUSSION

Male mice

In this experiment, observations were made of drugs that affect the autonomic nervous system in experimental animals rats and mice to see the ratio given by the class of drugs that inhibit or stimulate the work of the sympathetic nervous system and the parasympathetic nervous system, which is a nervous system that works under the autonomic nervous system.

3 male mice were provided in this experiment. In the treatment given to the first male mice by entering the drug metochlororamide which is a drug used to treat stomach problems. In this observation, metochlororamide was given orally and after a few minutes the mice were treated, giving the effect of tremors

or convulsions that occurred at 10 to 50 minutes.

The effect of metochlorpramide on intestinal motility does not depend on innervation of the vagus nerfus, but is inhibited by cholinergic drugs. From these observations it can be seen that metochlorpramide exerts pharmacodynamic effects on the parasympathetic nervous system.

The second mouse was given adrenaline by injecting the drug in the stomach. Adrenaline is a drug that treats allergic reactions and anaphylic shock. The effects experienced include diarrhea and diuresia at 10 to 30 minutes.

In the second trial mice given adrenaline had the effect of diarrhea and diuresia, which showed a pharmacodynamic effect that adrenaline was a direct-acting adrenergic agonist drug which was characterized by various effects.

Adrenergic administration also has an effect similar to stimulation of the adrenergic nerves. Adrenaline's vascular effect mainly on the small arterial and precapillary sphincters, but large veins and arteries are also affected, skin, mucosal and renal vessels are constricted due to receptor activation by adrenaline [2].

In the 3rd mice, the drug given was pilocaprin, which is a drug that can shrink the pupil of the eye and treat gloucoma. The drug is administered using dispo, which is injected intraperitoneally. At 10-20 minutes the effects caused by mice include miosis, at 0-10 and 20-40 minutes it gives the effect of diarrhea, diuresia At 20-40 minutes, tremors at 10-20, saliva at 10-40 and sweating at 0 -60 minutes.

After the administration of the pilocaprine drug, it can be observed through the effect given where the 3rd mice given the pilocaprine give a cholinergic effect which is generated which also includes stimulating or

stimulating glandular secretions, so that it can trigger hypersalivation so that more saliva or saliva is released as it is occurs in the 10-40th minute.

Female mice

Since we only have one female mouse, the treatment we do is only injecting metochlorpramide. After the drug was put into the body of the mice, the effects experienced by the mice included miosis 0-40 minutes, diarrhea 20-30 minutes, diuresia 20-30 minutes, tremor 10-20 minutes, vasodilation 0-10 minutes and 20-30 minutes and saliva 0-10 minutes and 30-40 minutes.

CONCLUSION

The conclusions of the research on the Autonomous Nerve System, namely the effect experienced by the effects of male and female mice when administering the drug have a stimulating and inhibiting effect on the sympathetic and parasympathetic nervous systems in animals, with this drug given in certain doses will have an impact on experimental animals.

The administration of the drug to experimental animals, namely mice (*Mus musculus*), was carried out by intraperitoneal and oral methods which could cause several effects, such as tremor, miosis, saliva, sweat, vasodilation, diarrhea and dieresis. Adrenergic agonist drugs of the sympathetic nervous system have the same effect as cholinergic antagonists on the parasympathetic nervous system. Meanwhile, drugs for cholinergic agonists in the parasympathetic nervous system have the same pharmacodynamic effect as cholinergic antagonists in parasympathetic.

The observations in this study indicate that the administration of metoclopramide to male and female mice has the effect of tremor, miosis, diarrhea, dieresis, vasodilation, saliva and sweating

Test of Stimulative Effects Generated by some Drugs on the Sympatic and Parasympatic Nerve Systems in Tried Animals

that occurs for 60 minutes. For the administration of adrenaline to mice, it has an effect in the area and diuresis and for the administration of pilocarpine to mice it has an effect felt by mice, namely miosis, diarrhea, diuresis, tremor, vasodilation, saliva and sweating which were observed for 60 minutes.

Adrenergic agonist drugs of the sympathetic nervous system have the same pharmacodynamic effect as antagonycholinergic drugs on the parasympathetic nervous system. Meanwhile, agoniscolinergic drugs in the parasympathetic nervous system have the same pharmacodynamic effect as cholinergic antagonists in parasympathetic.

As a recommendation given to this experiment, the laboratory is expected to be able to provide materials that will be used so that later the practitioner does not experience a shortage of material during the experiment and adjusts the practicum time so as not to use hours outside of what has been scheduled.

REFERENCES

- [1] Campbell, Neil A. Jane B. Reece, and Lawrence G. Mitchell. 2004. *Biology* 5th Edition Volume 3. Erlangga. Jakarta,
- [2] Damayanti R. 2000. Effect of hydrocortisone and adrenaline on the response pattern of immunocompetent cell mobilization in white rat blood. Surabaya. Thesis,
- [3] Ganiswarna, S., 1995, *Pharmacology and Therapy*, 4th edition, 271-288 and 800-810, Department of Pharmacology, Faculty of Medicine, University of Indonesia, Jakarta.
- [4] Halwatiah. 2009. *Physiology*. Alauddin Press. Makassar.
- [5] Irianto, Koes. 2013. *Anatomy and Physiology for Students*. Bandung: Alfabeta
- [6] Mycek., Mary J. 2001. *Pharmacology Picture Review* 2nd Edition Jakarta: Widya Medika.
- [7] Neal, MJ 2006. *At a Glance Medical Pharmacology* Fifth Edition. Jakarta: Erlangga Publisher. pp. 85.
- [8] Pearce., Evelya C. 2004. *Anatomy and Physiology for Paramedics*. Jakarta: Gramedia.
- [9] Sastradipradja D, 2003. *The Use of Experimental Animals in Research*. : Bogor: Lartude Agriculture.
- [10] Schulze-Delrieu K. Drug therapy. *Metoclopramide*. *N Engl J Med*. 1981; 305 (1): 28 - 33. Tjay and Rahardja K. 2002. *Essential Medicines*. Prolex Media Kompotindo Jakarta: Gramedia.
- [11] Sulistia. 2009. *Pharmacology and Therapy*. Edition 5. Jakarta: Faculty of Medicine, UI
- [12] Stringer, Janet L. 2009. *Basic Concepts of Pharmacology* Book Medical PublishersEGC: Jakarta
- [13] Tjay and Rahardja K. 2002. *Essential Medicines*. Prolex Media Kompotindo Jakarta: Gramedia.