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THE NEGATIVE EFFECT OF MERCURY IN COSMETICS ESPECIALLY IN BRAIN CELLS AND COLLAGEN TISSUE QUANTITY THAT RECOVERY WITH NANO-GOLD

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AUTHORS' CONTRIBUTIONS

This work was carried out in collaboration among all authors. Author TT designed the study, performed the statistical analysis, wrote the protocol and wrote the first draft of the manuscript. Authors IGMS and AB managed the analyses of the study. Author AS managed the literature searches. All authors read and approved the final manuscript.

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ABSTRACT

The pre-clinical research has been done to get empirical date the real of negative effect of mercury that used in cosmetics (mercury face cream). This research used 24 animals Mus Musculus divided into 6 groups; Control group; Mercury group; Nanogold 5ppm; Nanogold 10 ppm; Nanogold 15ppm and Nanogold 20 ppm. After adaptation two weeks All animal treat by mercury face cream for a week, except control group. After this treatment, 4 class continuous by recovery with nanogold 5, 10, 15, and 20 ppm for 4 weeks. One group that call mercury group killed to investigate effect of mercury face cream. Mercury had cause damages of fibroblast and reduce collagen quantity in skin tissue at previous research. This research investigated haw impact mercury in face cream at brain cells and collagen quantity of brain tissue if mercury exposure in skin area. The treatment continuous with nano-gold face cream to recovery and reduce these damages. HE staining used to analysis brain cells condition and Van Gieson staining used to analysis collagen quantity. The conclusion that a week mercury exposure caused many damage of tissues including collagen tissue, brain cells and others connecting tissue in brain. Recovery for 4 weeks with nanogold at variance concentration (5, 10, 15, and 20 ppm) reduce brain damage, especially brain cells and collagen tissue step by step near normal condition. The role of concentration of nanogold was real. The increase nanogold concentration give recovery be better. The impact of this research nanogold sweet material to substitute mercury that very dangerous material in cosmetics. Nanogold in the future as the best material in cosmetics formulation.

Keywords: Mercury; cosmetics; brain cell; collagen; recovery; nanogold.

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1. INTRODUCTION

Today mercury steel found in many kinds of cosmetics, for ex ample day cream, night cream, body lotion, and moisturizing cream [1]. Mercury used as whitening material in cosmetics is be very dangerous. In the fast time the negative effect of mercury is not yet seen, because the skin showed smooth and white. Mercury pressure melanocyte cells activity that produced melanin one of skin pigment [2]. Skin with little pigment show white and beauty, this condition that liked many women. The second period that this condition change with hyperpigmentation, there are many spots in the face skin. Melanocyte cells have not been pressure with mercury in the same concentration or smaller in the case stopped using cosmetics.

The especially effect of mercury in cosmetics at brain cells and collagen tissue is a main-study in this research. The aim of the research to educate peoples that using cosmetics with mercury content is very dangerous than must be stopped now [3]. Beauty clinic that steel using mercury as whitening material that give changes drastically must be stopped. The reality women very interesting with instant treatment to get beautiful. Beautiful not identic with white skin. White skin that not health was given many dangerous and damage than continuous causes many diseases [2,3].

Brain is main organ that handle sensory system center have important role to control all of human and animal activity. How dangerous mercury is for your brain? What happens to your brain cells if when they're exposed to mercury? What happened that nanogold used to recovery, Is it have significant changes to make healthy brain cells, all of question that answer in this research. Effect of mercury in cosmetics in skin had explanation inhibits proliferation of fibroblast and reduce collagen quantity [2]. Cerebrum is a part of brain have function as thinking center, sensory center and personality. The main study of this research is investigation the part of the body that the most important organ that is brain. Including in the brain organ that is brain cells and collagen tissue.

Glia cells are including brain cells in the center of human neural center system have many functions and complication relation with human activity. The scientist fond the relation glia cells that evolution to be astrocyte with cognitive ability. This conclusion resulted after the scientist transplantation human astrocyte to rat brain, the rat cognitive ability significantly increased. The evolution of glia cells is the key event that resulted increasing cognitive function, its cause that human and other species are be different [4]. Exposure to electric current in the media freshwater and seawater cause lyses of neural cells, subarachnoid brain blooding, and *organic brain syndrome* [5].

The effects of hypobaric exposures up to 7 days after traumatic brain injury (TBI) significantly worsened cognitive deficits, hippocampal neuronal loss, and microglial/astrocyte activation. Oxygen exposure during hypobaric exposure exacerbated spatial memory deficits, while maintaining physiological oxygen concentration worsens long-term cognitive function and neural-inflammation [6]. Beta glucan of saccharomyces cerevisiae can increase the number of neural cells at substantia-nigra, part in the Parkinson model of Wistar rat strain [7].

Potential biomarkers that fond in traumatic brain injury (TBI) are UCH-L1 and GFAP that resulted from neuronal cells and astrocyte cells that loss. Ubiquitin Carboxy-terminal hydrolase L1 [UCH-L1] resulted from neuronal that lyses and glial fibrillary acidic protein [GFAP] from astrocyte [8]. Breakdown product of brain-specific proteins released into serum is GFAP that can measure by computed tomography and magnetic resonance imaging. This protein detected as part of the pathophysiological response after traumatic brain injury (TBI) [9]. GFAP and S100β are found in glial cells that break and are released into blood serum after a traumatic brain injury (TBI) case. Reality the clinical utility of S100β as a biomarker that release from breaking bone cells (osteoblast). With computed tomography (CT) scan ability of GFAP and S100 β are detected as biomarker in the patient cases including intracranial lesions and extra-cranial injuries on head [10].

Memory-based tasks are independent by deployment history, combat exposure, symptoms of posttraumatic stress disorder and depression but dependent with neurocognitive functioning [11]. Injury to central myelin contribute to continued degeneration of axon after traumatic brain injury (TBI). The damage of the myelin sheath and oligodendrocytes of the optic nerve fibers may contribute to the continuance of axonal loss [12].

Many materials and many tragedies that cause brain cells damage, and these damages can reduce step by step with many treatments. This Research specially to get information what happen if mercury used in topical skin for example using in cosmetics, and continuous recovery by nanogold. If the damage was occurs to the other part of the body especially in the brain cells and collagen tissue in this organ, that this damage can recovery to with nanogold treatment. The result of this research used to normalization many

destructions that been occur at victims of mercury exposure in cosmetics. Until now They are not been get solution to recovery and fix their face damage. If nanogold is a solution for this problem, was happy news for all. Manny diseases caused brain damage for example Alzheimer's disease, autism, brain cancer get hope to recover and fix again.

2. METHODOLOGY

Material used in this research: separate glass instrument, separate embedding tissue treatment, microtome, separate staining histology-chemistry treatment, 24 mice (Mus Musculus strain) put brain organ, HE staining, Van Gieson staining, microscope Axio Imager A2 with camera Axiocam ICc 1 , software Axiovison Rel 4.8.

This research needed 24 mice (Mus Musculus strain), adapted within 2 weeks. These mice be divided in 6 groups, 1 group used control and 5 others used treatment groups. Treatment groups exposed to mercury by lubricate mice back with mercury facial cream and control group lubricate with placebo facial cream. The formula of placebo facial cream refers to the common face beige and mercury facial cream made from placebo that added mercury ion Hg^{2+}0,1ppm. After week treatment, one of treatment groups executed and analysis to get information what happen in the mice's brain after exposure to mercury. 4 treatment group recovery by nano-gold facial cream. Nanogold facial cream made from placebo facial cream that added colloidal gold or nanogold in variance concentration 5,10,15, and 20 ppm. Nano-gold used recovery skin damage that effect of mercury in cosmetics (3). After 4 weeks recovery All of these groups (5, 10, 15, and 20 ppm Nanogold) executed and analysis to get information about recovery process had begun. Mice's brain cells and all of condition collagen tissue capture by compared every variance concentration.

Method: Mice brain of control and treatments group put and marinated in formalin 13% concentrate. Every mice brain embedding in liquid paraffin to form sample blog paraffin. After sample blog paraffin harden, cut with microtome instrument to get 4 microns slide sample. The slide sample prepare to staining process by marinated degrading alcohols solution in concentrate. Begun alcohol 10% concentrate, 20%, 30%, until absolute alcohol and the end in the xylol solution. After these process sample stained by 2 kind of staining. HE staining to get brain cells picture and Van Gieson's staining to explore collagen quantity picture. Microscope with camera and software used to get data. Analysis of the date used Statistic by multivariate analysis MANOVA to get relation of each variable.

3. RESULTS AND DISCUSSION

Microscope picture Histology-chemistry of Brain Tissue of Mus Muscullus.

3.1 Microscope Picture of Brain Tissue by HE Staining

HE staining used to bright of brain cells because this staining is acidic stain character and cells character is based. The binding of cells and HE staining is ionic binding or base-aced interaction, the picture of brain cells showed ferry clear because maximal absorption of HE staining occur. The quantitative date of brain cells computed the number of cells in the certain area. In this research the certain area is 80.000μm^2. The brain cell in the Fig. 1 part a. is very clear as red circle with transparent divider. The size of each brain cell was different, there are big circle and little one. The part b of the Fig. 1 red circle of brain cell not clear because many cells die. This shows the bad effect of mercury on cells. The subsequent effect on the number of cells per area also decreased compared to part a Fig. 1. The number of brain cells each 80.000 μm2 can see at Table 1. The number of cells was increased in the recovery group with nanogold in the part c of Fig. 1. More clearly from Table 1. the number of cells in the mercury group was less than the normal group, while the treatment group with nanogold had more cells than the normal group and the mercury group. In the Fig. 1 part c, everyone can see new cells growing as red circles bordered by transparent areas. This shows the effect of nanogold in the recovery of cell damage than cell growth again. The greater the nanogold concentration the mor new cells will grow. This shows a very strong role for nanogold in cell regeneration. Nanogold is very important for cosmetic materials as a solution and substitute for mercury as whitening. The new cells are young cells that are brighter and whiter in color. It's a nanogold realistic base for future whitening in modern cosmetic formulas.

3.2 Microscope Picture of Brain Tissue by Van Gieson's Staining

Special staining to get collagen seat picture used Van Gieson's staining. Collagen absorption with this staining very good and stabile. The collagen quantity calculation with Axiovison Rel 4,8 software. The percent area covered with collagen is the date get from this software. Degradation of collagen decrease the percent area that show many hole's area without collagen. Collagen area show with red area in this picture and hole's area show white area. The percent

area gets from the red area be divided by all certain area. The certain area is 80.000µm2. The Quantitative date of percent area from control and treatment group analysis by statistic with MANOVA. This analysis to get the different significant of each group. The date percent area of each group can see at Table 2.

This staining the collagen is red and is an area outside the cell. With the software the collagen area is determined and compared across a certain area. The data on the percentage of collagen area is presented in Table 2. Fig. 2 part a show the collagen density of the normal group which looks red and dense.

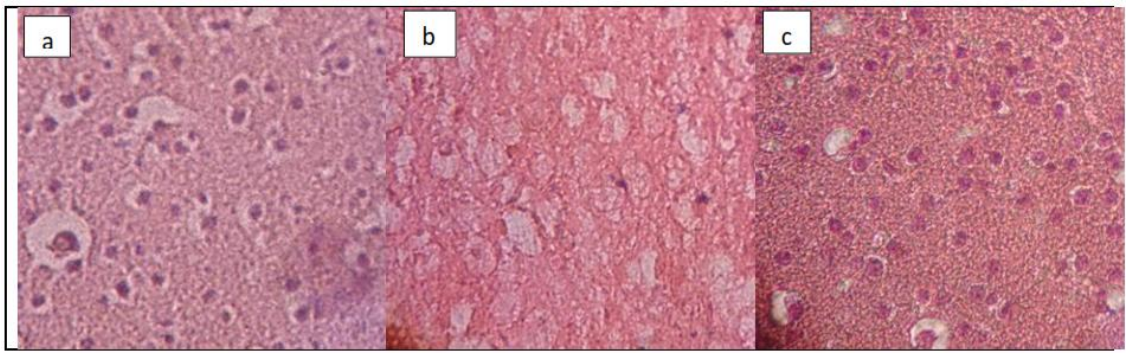

Fig. 1. Microscope picture of brain cells, a. the picture of control group, b. the picture of treatment group with mercury without recovery and c. the picture of treatment group with mercury than continuous recovery with nanogold

Table 1. The number of brain cells control and group treatment of mus musculus

Group	The Number of Brain Cells in the 80.000µm^2 of area			
	Rep-1	Rep-2	Rep-3	Rep-4
Control Group	31	29	30	30
Treat-Mercury	8	7	9	7
Recovery-NG-5	11	13	12	14
Recovery-NG-10	14	16	17	17
Recovery-NG-15	22	27	24	26
Recovery-NG-20	33	32	30	29

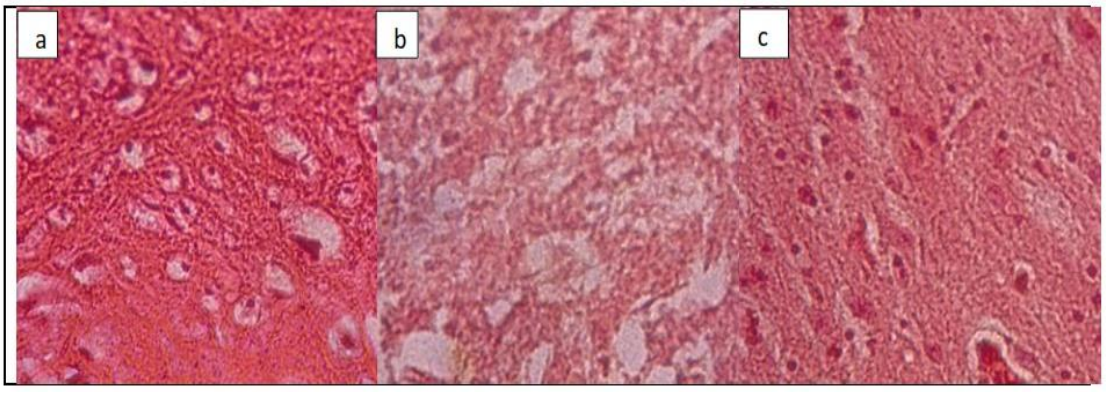

Fig. 2. Microscope picture of collagen, a. the picture of control group, b. the picture of treatment group with mercury without recovery and c. the picture of treatment group with mercury than continuous recovery with nanogold

Table 2. The percent area collagen control and group treatment of mus musculus

Group	The Percent area of collagen in the 80.000µm^2 of area			
	Rep-1	Rep-2	Rep-3	Rep-4
Control Group	62.23	60.76	67.20	60.37
Treat-Mercury	25.78	28.88	26.30	22.56
Recovery-NG-1wk	34.22	35.67	38.54	33.30
Recovery-NG-2wk	42.34	44.45	42.34	46.30
Recovery-NG-3wk	56.78	55.23	58.23	53.23
Recovery-NG-4wk	65.23	66.45	69.50	63.56

This is different in Fig. 2. Part b where the collagen density decreases and collagen color fades. This is due to the damage caused by mercury and has not been recovery as shown in Fig. 2 Part C. In this picture be can see that the collagen density returns to normal as well as a brighter color than the mercury group. Likewise, the percentage of collagen area in the mercury group was lower than in the control group. This indicates that mercury decreases the area of collagen or causes collagen damage. After recovery with nanogold the area of collagen was increased. The greater the nanogold concentration used, the greater the area of collagen produced.

Collagen is an important protein for skin elasticity, so the material that triggers skin growth is very suitable for cosmetic materials. With the tighter collagen, the skin will stay young. This is very attractive to cosmetic users. Thus, nanogold is very suitable as an antiaging material in modern cosmetics in the future.

HE staining used to know reduction brain cells showed in the Fig. 1, part b. The number of brain cells reduction significantly after mercury exposure compare control group Fig. 1, part a. Degradation process begun with interaction mercury and amino-acid (part of protein) that contain thiol-group(-S-H) or disulfide binding. This interaction resulted breaking of the binding and forming free radicals. The free radicals attack tissue, cells, membrane, blood, etc. The result of these attack, its form new free radical. The forming free radicals repeatedly to damage all others. This event detected with loses brain cells. The hole area is cells place that damage and death. Fig. 1part c. is recovery these damage with nanogold. Brain cells grow and detect again.

Van Gieson's staining used to know collagen quantity. The reduction of collagen after mercury exposure process showed in the Fig. 2, part b. The percent area covered collagen decreased in this figure compare control group in part a. Degradation collagen process occur at the time that mercury attack this protein. Many binding breaks and result free radicals. Free radicals attack collagen tissue in these areas. The damage of collagen tissue detects by hole-area without collagen. Collagen area show by red area and the hole-area without collagen show by white area. Fig. 2part C is recovery process of damage collagen tissue with nanogold. Collagen quantity increase that show by fill of hole-area with new collagen. The new collagen that form is near control group condition part a.

Endogenous stem cells treatment is not can repair traumatic brain injury, but exogenous transplants can repair and remarkable traumatic brain injury and supporting glia cells. The potential technology to clarifying and cells reprogramming developed to generate autologous glia and neurons cells to repair many brain damage [13]. The damage brain cells especially glia and neuronal cells caused oxygen and nutrient supply stopped at few episodes. The condition with oxygen exceeds its supply induced hypoxia and continuous with neuronal cells death and loss. Inadequate oxygen supply causes many anaerobic metabolisms, increase respiration, angiogenesis, erythropoiesis and peripheral tissue damage. This condition spark inflammation of glia and neuronal cells, body growing disturbed, and inflammatory cytokines [14].

The effect of prenatal alcohol exposure in humans is damage in central nervous system (CNS), contribute detrimental effects, and particular brain regions damage. The mechanism of this condition begun that alcohol exposure increases oxidative stress, followed mitochondrial damage that correlation with growth factors activity of glia cells. This damage contributes cell adhesion molecules, gene expression and impaired function neural communication be changes, than cause abnormalities of neural plasticity, memory, learning ability [15].

Methyl mercury is a neuronal-toxicant that cause abnormal neuronal differentiation and damage several brain developing processes, and disturb epigenetic regulation in MicroRNAs (miRNAs). Target of miRNA- defined in lines of play role in specific for neuronal differentiation be axon guidance or neuronal-trophyne regulated signaling [16]. Human get mercury

neurotoxin pollutant through by consumption of fish with form organic methyl mercury.

The highest mercury accumulation occurs in 14 months of exposure, in this time range the main organ have content mercury. In the Kidney content 511 ng/g, in the liver 77 ng/g, in the hair 733 ng/g, and in the brain 35 ng/g [17]. Mercury in cosmetics cause skin tissue damage including fibroblast proliferation and collagen quantity [18]. Recovery and normality of fibroblast proliferation and collagen biosynthesis with Nano-gold occur 4 weeks treatment by a week mercury exposure treatment in mice as animal test [19]. Heavy metal especial Mercury cause negative effect at human rheumatoid synovial cell proliferation and collagen synthesis [20]. The damage that caused mercury exposure begun formed free radical occur that mercury attach and destruction tissue compounds. Recovery by Nano-gold can be done because Nano-gold have high activity to reduction free radicals [21]. Gold Nanoparticles can reduce inflammation of brain cells and reduce apoptosis of this cells, so the regeneration of these cells occurs step by step and recovery process be done [22]. Gold Nanoparticles used to recovery mercury damage in skin area [3], recovery in brain area. The manufacture of cosmetics with nanogold was initiated and patents were drafted [23]. This is to replace mercury which is harmful to the liver and kidneys in preclinical trials [24]. Mercury also inhibits cell proliferation and degrades collagen [25], including inhibiting fibroblast proliferation and decreasing the quantity of collagen in the skin [26]. However, until now, cosmetics containing mercury are still widely circulated [27]. Mercury in cosmetics triggers the formation of free radicals that are harmful to health and the nanogolds reduce these free radicals [28]. This is what underlies the replacement of mercury with nanogold in cosmetics. Nanogold also forms a complex with glutathione to synergize in maintaining the body's immune system [29].

4. CONCLUSION

Mercury that exposure to skin can caused tissue damage including collagen and brain cell, that is can be used to warning cosmetic using in the world. Heavy metal especial mercury caused negative effect at cell proliferation and collagen biosynthesis. This begun by forming free radical that attach and destruction tissue compounds in the body. Recovery by Nano-gold can be done because Nano-gold have high activity to reduction free radicals. Nanogold is solution material to reduce negative effect of mercury. In the future cosmetic with nanogold substitute mercury as whitening material. Nanogold is not give negative effect, nanogold will build healthy skin and health body around.

CONSENT

It is not applicable.

ETHICAL APPROVAL

Ethical approval has been taken from the animal ethics committee to carry out the study.

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COMPETING INTERESTS

Authors have declared that no competing interests exist.

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