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Chapter

Total Antioxidant from Herbal Medicine as a Possible Tool for the Multifunctional Prevention of Muscular Atrophy

Viani Anggi

Abstract

Muscular atrophy is one of disease by the loss of skeletal muscle mass. So, by the loss in muscle often causes rapid muscle atrophy and the occurs during injury and illness its causes immobilization in spinal muscle mass. Usually, the impact factor of the nervous system in musculoskeletal is caused by aging, immobility, malnutrition, medication and even the range of injuries disease impact by the nervous system. To meet the needs needed by the loss of skeletal, we need high total antioxidant from herbal medicine as multifunctional potentially prevention of muscular atrophy condition. Antioxidants are agents that can slow down or prevent oxidation process and protect cells system from the damage of cell by the loss skeletal in muscle mass. One of herbal medicine is *Abelmoschus manihot* L. Medik From Palu of central Sulawesi as a possible multifunctional prevention of Muscular Atrophy, where the total antioxidant value is 3,45 mg/mL.

Keywords: total antioxidant, herbal medicine, multifunctional prevention, muscular atrophy

1. Introduction

Muscular atrophy is one of disease by the loss of skeletal in muscle mass. The muscular atrophy recessive autosomal in neuromuscular with characterized of alpha motor neuron in the spinal cord [1]. The neuromuscular disorders are one factor genetic of infant mortality [2]. The spinal muscular atrophy deletion or mutation the Survival motor neuron 1 (SMN 1 gene), reduction of levels functional survival motor neuron 1 (SMN 1 gene) and also resulting selective death of spinal motor neurons system in a pathway, it's depends by the age of onset, symptoms and maximum function achieved [3]. By the age at the onset it causes at birth: Neuromuscular disease, congenital myotonic dystrophy and spinal muscular atrophy, other causes are systematic septicemia-induced disease, lung damage, intracranial pathologies, infection of the central nervous system, disorders of the peripheral nerves, disease of the neuromuscular junction, Prader-Willi syndrome and drug intoxication during pregnancy or delivery system and after 6 months of age were the neuromuscular disease: spinal muscular atrophy types II and III, polyneuropathies, childhood myasthenia gravis, muscular dystrophies and metabolic myopathy and besides that in other causes were congenital heart disease, malnutrition, rickets, metabolic diseases, nephropathies and lung diseases [4, 5]. The clinical prognosis of

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spinal muscular atrophy is variable and depends on types of spinal muscular atrophy continuous spectrum with the age of death by infancy to normal life expectancy condition system on cell pathway system [6]. The Muscular atrophy its described with characterized generalized muscle and atrophy in the proximal limb muscle and phenotype by four grades of severity, where the spinal Muscular Atrophy I, spinal Muscular Atrophy II, spinal Muscular Atrophy III and spinal Muscular Atrophy IV, it's all depended by onset and motor spinal function [7, 8]. The muscular atrophy disease by the control mutation in the homozygous of survival motor neuron α (SMN 1) gene. The skeletal of muscular atrophy it's adverse consequences and the mechanism such as wasting or decrease of injury time. Lack of use in the spinal muscular atrophy and event disease category of spinal muscular atrophy. The spinal muscular atrophy it's usually considered by chronic diseases such as poliomyelitis, Diabetes mellitus, cancer, renal failure or pulmonary obstruction [1].

To activation of spinal muscular atrophy, we need the process to activation of the distinct pathway (ATP) in proteolysis pathway. The condition of spinal muscular atrophy it's depends on the level of muscle protein nutrition system. To reduce the fiber muscle we need synthesis protein to innervate proximal hindlimb muscles and medical motor neurons axial muscles [9]. Mitochondrial is important in skeletal muscle to activation of function and subpopulation involved in cellular functions. Mitochondria play in role key on muscle fibers to the regulation of myonuclear apoptosis and serving uptake the calcium [10]. Mitochondria also continuously produce superoxide radicals and dismutated into hydrogen peroxide (H_2O_2), where H_2O_2 is a relatively and diffuse freely with cytosol, it's very important as signaling to the molecule on cell, to affecting multiple control of the cell cycle, uptake to cellular stress response, activation energy metabolism and also to the expression of numerous redox-sensitive genes in spinal muscular atrophy disease [9].

2. Prevalence, incidence and carrier frequency of muscular atrophy

According to the worldwide about a study into the prevalence and incidence of spinal muscular atrophy, where approximately 1–2 per 100.000 people and incidence around 1 in 10.000 live births have been estimated with the spinal muscular atrophy type I accounting for around 60% of all cases and estimation of the incidence of all types of spinal muscular atrophy of around 10 in 100.000 (1 in 10.000) live birth is cited [11]. Every incidence is a factor from a number of new cases of the disease in a particular time period. The evaluation of the incidence of all type SMA combined it's around 8 per 100.000 live births. The incidence of spinal muscular atrophy type I is around 4–6 in 100.000 and for the type II and III it's a high incidence combined 10,6 per 100.000 and for the gender, it's a nearly even split male and female [12]. The indicated difference of spinal muscular atrophy types is the between ethnicities and differences in health system clinically diagnosed. The prevalence in Indonesia of neuromuscular in RSCM hospital from January – December 2017 is 2,6% of all patients who come to the neurology outpatient ward. The five most who have neuromuscular disorders are neuropathy peripheral, Duchenne muscular dystrophy, spinal muscular atrophy, Guillain barre syndrome and chronic inflammatory demyelinating polyneuropathy [13].

3. Genetics of spinal muscular atrophy

Spinal muscular atrophy is a defect in survival motor neuron 1 (SMN 1) and it's gene localized to 5q11.2-q13.3). SMN gene (SMN 1 and SMN 2) on chromosome

5q13 and the homozygous deletion of the SMN 1 gene result in Spinal muscular atrophy. Besides that, the SMN 2 gene it produces mostly a shortened, unstable the survival motor neuron mRNA and also to alternative splicing, a small amount of full – length on functional SMN mRNA. The SMN 2 gene is a good prognostic of the spinal muscular atrophy in clinical severity. The clinical severity management of spinal muscular atrophy disease is supportive to increase the survival motor neuron expression levels in motor neurons cells system. So, the management of spinal muscular atrophy depends on increase SMN expression levels in motor neurons [3].

The survival motor neuron 1 gene it should be sequenced mutations if both full SMN 1 present of diagnosis on spinal muscular atrophy is highly, but the SMN 1 gene should be sequenced if the striking typical phenotype, where if sequencing indicates and intact SMN 1 gene of phenotype suggestive of spinal muscular atrophy neurogenic. The survival motor neuron 2 gene should be routinely assessed and it's important to factor system influencing the severity of the spinal muscular atrophy phenotype [1].

4. Molecular oxidative stress factor of muscular atrophy

Factor oxidative stress of muscle atrophy it's important to maintenance and quality to the rehabilitation of disease. The skeletal of muscle atrophy need continuously produce oxidants like as a reactive oxygen species (ROS) and reactive nitrogen species (RNS) to an imbalance of skeletal muscle mechanism process. The soluble atrophy it's produced different oxidative stress state species such as O_2^-, H_2O_2 and OH^-. Where, it also needs antioxidant species state such as catalase, glutathione peroxidase (GPx) and superoxide dismutase (SOD) and the last to imbalance denominated of oxidative stress, it's can produce oxidative damage in lipids, Deoxyribonucleic acid (DNA) and protein to impairing functional protein factor of cellular system [14].

Generation of ROS could uptake of oxygen, activation of NADPH oxidase and to production of the superoxide anion radical, see the reaction:

$$2O_{2+}\ \mathrm{NADPH} \overset{\text{oxidase}}{\rightarrow} 2O_2^- + \mathrm{NADP}^+ + \mathrm{H}^+ \quad (1)$$

Where O_2^- is converted to H_2O_2 (Eq. (2) by SOD

$$2O_{2+}\ 2\mathrm{H}^+ \overset{SOD}{\rightarrow} H_2O_2 + O_2 \quad (2)$$

The skeletal of muscle atrophy could inactivity increase of mitochondrial reactive oxygen species (ROS) production on the ways. The mitochondrial could uptake of calcium and increase mitochondrial levels state of fatty acid hydroperoxides and the last depressed protein could transport into the mitochondria system. So, if the mechanism responsible, it's could increase mitochondrial fission [9].

The observation of muscle mass-specific overexpression of Peroxisome proliferator-activated receptor-y-coactivator-1α (PGC-1α) and the master regulator of mitochondria biogenesis could prevent activation of catabolic system and disuse of muscle atrophy system. The Peroxisome proliferator-activated receptor-y-coactivator-1α (PGC-1α) is mediated pathway and focuses on the role PGC-1α in the skeletal spinal muscular atrophy system by immobilization system. The Peroxisome proliferator-activated receptor-y-coactivator-1α (PGC-1α) is the master transcription stimulates of mitochondrial biogenesis pathway system with up the regulating system of the nuclear respiratory factors (NRF-1,2) and mitochondrial

transcription factor A (Tfam) system, so it leads to increased mitochondrial DNA replication system and gene transcription system [15]. The Peroxisome proliferator-activated receptor-y-coactivator-1α (PGC-1α) to appears key to the role-play a protective against of muscular atrophy linked skeletal muscle deterioration. The Peroxisome proliferator-activated receptor-y-coactivator-1α (PGC-1α) interacts with the nuclear receptors and activate transcription factors to activated their target gene. The activity to responsive multiple stimuli including calcium ion, Reactive oxygen species (ROS) and ATP demand pathway system on the cell system in the spinal muscular atrophy. The metabolic stress mediated by PGC-1α downregulation plays a major role in muscle atrophy and to adaptation the soleus to mice hindlimb unloading (HU) in the defuse, we need antioxidant treatment (Trolox). Which, the HU caused of reduction in the cross-sectional area, redox status alteration (NRF2, Superoxide dismutase1 and catalase up-regulation) and the autophagy (Beclin1 and P62 mRNA up-regulation) [16]. The attractive of PGC-1α states in muscle mass could restore and promote the muscle metabolic system when normal physical activity impossible. The observation of the muscle fiber – specific event until overexpression of the attractive of PGC-1α states, where a master regulator of the mitochondrial biogenesis, to prevent activation produce of the catabolic system and also disuse muscle atrophy.

5. Antioxidant mechanism and function

The natural antioxidant is one important to underlying to spinal muscular atrophy system. The natural antioxidant could effect to exercise the health-promoting increase muscle defenses [17]. The natural antioxidant which role-plays to activation integrity on the cell and to prevent the free radical configuration tissue damage of muscle atrophy to normal healthy condition system of muscle atrophy pathway [18].

The natural antioxidant increasing antioxidative defenses and develop a synthesis of endogenous enzymes or increased antioxidant utilization, practice to maintain optimal body function to especially of spinal muscular atrophy in the redox condition on cell [19]. The function from natural antioxidant: it reduces the free radical of spinal muscular atrophy, stimulates the growth of normal cells, to protects the cell against the premature and abnormal aging condition of spinal muscular atrophy, helps fight the age-related molecular degeneration of spinal muscular atrophy and the last to supports the body immune system [17]. The natural antioxidant is powerful electron donors and also to the reaction of free radicals to target molecules breaking damaged on skeletal muscular. The lipid phase of chain-breaking antioxidant can scavenge the radicals in membranes and lipoprotein particles to preventing lipid peroxidation of skeletal muscular atrophy. The lipid phase such as tocopherols, ubiquinol, carotenoids and flavonoids and the aqueous phase such as ascorbate, urate, glutathione and other thiols [20, 21].

6. Flavonoids are group of antioxidants

Flavonoids are a group from based on natural substances by a variable phenolic structure, where are found from fruits, vegetables, grains, bark, roots, stems, flowers, tea and wine. Flavonoids are potential to anti-oxidative, anti-inflammatory and anti-mutagenic on spinal muscular atrophy disease [22]. As an anti-inflammatory, we need of agent system, where the COX is an endogenous enzyme with catalyzes function, which the conversion of arachidonic acid into prostaglandins and thromboxanes,

where the enzyme exists in two isoforms: COX - 1 is a constitutive enzyme and is responsible for the supply of prostaglandin and Cox – 2 is an inducible enzyme and is expressed an inflammatory stimulus and the stimulus prostaglandin to induction of inflammatory and pain. By using, the flavonoids can activate the molecular docking and knowledge bioinformatics in preventing chronic disease like as spinal muscular atrophy and to application and manufacturing in pharmaceutical medicinal industry [23]. Flavonoids subdivided of subgroup depending on the carbon of the C ring on which the B ring, which the degree of unsaturation and oxidation of the C ring. The firs isoflavone, which in the B ring is linked position 3 of the C ring. Second, the neoflavonoids, which the B ring is linked in position 4. Besides that, the subdivided into several subgroups on the basis which the B ring is linked position 2 on the basis of the structural features of the C ring. Flavonol (e.g. Quercetin, myricetin), flavone (eg. apigenin, luteolin), flavonolols (eg. taxifolin), flavan-3-ols (eg catechin, epigallocatechin), flavovone [24] (eg. hesperitin, naringenin), anthocyanidin (eg. cynidin, delphidin), isoflavone (eg. genistein, daidzein).

7. *Abelmoschus manihot* L. Medik is one of herbal medicine

Abelmoschus manihot L. Medik is have highest total antioxidant (**Table 1**). The leaf plant is a tropical plant from china, which is trapped by the name Huangkui. Ethanobotanical uses and phytochemical analysis of *Abelmoschus manihot* L. Medik, where the preliminary study shows the presence of alkaloid, carbohydrates, tannins, steroid and glycosides [25].

Compound		Name
1	Hyperoxide/ Hyperin	Dihydroxyphenil)-3-{3R,4S,5R,6R)-3,4,5-trihydroxy-6(hydroxymethyl) oxan-2-yl}oxy-4H-chromene-4,5,7-triol
2	Isoquercetin	2-(3,4-dihydroxyphenyl)-5,7-dihydroxy-3{(2S,3R,4S,5S,6R)-3,4,5-trihydroxy-6-(hydroxymethyl)oxan-2-yl} oxychromen-4-one
3	Myricetin	3,5,7-Trihydroxy-2-(3,4,5)-trihydroxyphenyl-4-chromenone
4	Hibifolin	quercetin 3-beta-robinobioside; 3{(6–0-(6-Deoxy-alpha-L-mannopryranosyl)-beta-D-galactopyranosyl}oxy)-2-(3,4-dihydroxy phenyl)5,7-dihydroxy-4H-1-benzopyran-4-one
5	Quercetin	3-O-robinoside: Quercetin 3 –beta-robinobioside; 3-{(6-O-(Deoxy-alpha-L-mannopyranosyl)-beta-D-galactopyranosy} oxy)-2-(3,4-dihydroxyphenyl-4H-1-benzopyran-4-one
6	Coumarin scopoletin	7-hydroxy-6-methoxychromen-2-one

Table 1.
Some compounds isolated from the genus Abelmoschus manihot *L. Medik [26].*

8. Ethanomedicinal, phytochemical and pharmacological of *Abelmoschus manihot*

Ethanomedicinal, phytochemical and pharmacological profile of genus *Abelmoschus manihot* L. Medik where the genus *Abelmoschus manihot* L. Medik has been reported to used for several ethnomedicinal practices and also demonstrated diverse pharmacological activities and posses several phytochemical and nutritional properties as well as having and no adverse effect on living cells, their pods, seeds and leaves are reported to be used in pharmaceutical industries

and traditional remedies all over the world [26]. The protective effect on the total flavonoid of *Abelmoschus manihot* L. Medik on transient cereberal ischemia-preperfusion injury is due to activation of the Nrf2-are pathway, where the highest total flavonoids 788,56 mg/g) of all the different part, the protective effects of an extract of the total flavonoids of *Abelmoschus manihot* L. Medik on transient cereberal ischemia–reperfusion injury (TCI-RI) were investigated, these data suggest that to protects against TCI-RI by scavengin free radical and activating NRF2-ARF pathway (Nuclear factor E2-related factor 2 contributes to neuroptotective immune system, antioxidation, antifatigue and anti-inflamatory properties [27]. The bioactive compounds from *Abelmoschus manihot* L. Medik alleviate the progression of multiple myeloma in mouse model and improve bone marrow environment, where the *Abelmoschus manihot* L. Medik derived as a Huangkui capsules (HKC) represent a traditional Chinese medicine that has been widely applied to the clinical therapy of kidney and inflamatory disease by methods expressions of certain proteins were detected via western blotting, transcriptomic RNA-sequencing as well as RT-qPCR, where the result revealed that MM-Prone animals appeared to be protected following HKC treatment as evidence by a prolonged survival rate, which four of the nine flavonoid compounds (Hyperin/hyperoxide, HK-2; cannabiscitrin, HK-3, 3-O-kaempferol-3-O-acetyl-6-O-(p-coumaroyl)-β-D-glucopyranosid, HK-11, 8-(2-pyrolidione-5-yl)-3-O-β-D-glucopyranosid, HK-E3) suppressed osteoclastogenesis in murine raw 264.7 cells.HK-11 directly inhibited MM cells (ARP1 and h929) proliferation and induced G0/G1 cell cycle arrest, which may have involved suppressing β-catenin protein, increasing expression of IL-6 and TNF-α, as well as activating mature TGF-β1 and some other metabolic pathways [28]. *Abelmoschus manihot* L. Medik have supplementation as a Nephropathy system by methods a combined treatment of a high – fat diet and streptozotocin after unilateral nephrectomy and supplementation of *Abelmoschus manihot* L. Medik were tested, the results is preventive effects of the extracts on Nephropathy pathology system and changes on autophagy mitocondrial proteins were investigated to showed significant increase in fasting blood glucose, plasma creatinine, blood urea nitrogen and urinary albumin levels [29]. *Abelmoschus manihot* L. Medik as a Huangkui in Chinese, where as a traditional Chinese medicine, the Huangkui has been used for medication of the patients as a reduce inflammation anti-oxidative stress, improving immune response system, protecting renal tubular epithelial cells, ameliorating podocyte apoptosis, glomerulosclerosis and mesangial proliferation, as well as inhibiting on cellular and molecular mechanism [30]. So, with the natural antioxidant as a reduces the free radical of spinal muscular atrophy and stimulates the growth of normal cells. In Palu city of central Sulawesi Indonesia, where the plant is known as one of the raw based material of vegetables and is usually mixed with pulp.

9. Total antioxidant of *Abelmoschus manihot* (L.) Medik

This plant is believed to have medicinal based properties, because are many compound vitamins, like as: A, B1, B2, B3, C and E, compound the calcium, potassium, copper, zinc and many collagen. This plant also contains secondary metabolites like as: Flavonoids, Saponin and phonolite, where it has used as an antioxidant. The evaluate total antioxidant arrest activity using the DPPH (IC_{50}) of *Abelmoschus manihot* (L.) Medik extracts from Palu of Central Sulawesi, the method is displayed in **Table 2** and **Figure 1**, evaluate the potential activity of the test substances for the cytotoxicity against selected 4 T1 cell lines and Vero cell of *Abelmoschus manihot* (L.) Medik extracts from Palu of Central Sulawesi. The

Name of Test Substance	Antioxidant Activity DPPH IC_{50} (mg/mL)
Leaf *Abelmoschus manihot* (L.) Medik extract	3,45

Table 2.
The antioxidant activity DPPH (IC_{50}) of leaf Abelmoschus manihot *(L.) Medik [32].*

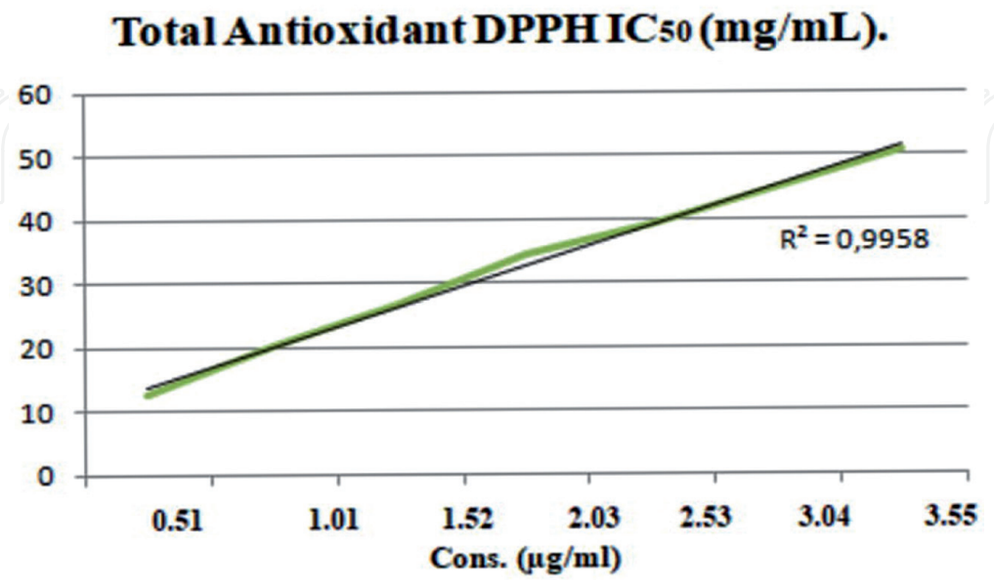

Figure 1.
Graph of total antioxidant of Abelmoschus Manihot.

cytotoxicity potential of various concentration of ethanol, ethyl acetate, N-Heksan extracts with CTC_{50} values of leaf *Abelmoschus manihot* (L.) Medik is displayed in **Tables 3** and **4** and **Figures 2** and **3**. Leaf *Abelmoschus manihot* (L.) Medik from Palu of Central Sulawesi extract plant shows the total antioxidant is 3,45 µg/ml from reports arrest of DPPH (IC_{50}) is displayed in **Table 2** and **Figure 1**. According to the criteria to the level of antioxidant power with DPPH (IC_{50}) method, where the extract of natural ingredients with IC_{50} < 50 µg/ml is potential. The in-vitro cytotoxicity effects of leaf *Abelmoschus manihot* (L.) Medik from Palu of Central Sulawesi, where carried with various concentrations to the breast cancer cell lines 4 T1 and have Potentially Toxicity, where the leaf of *Abelmoschus manihot* (L.) Medik of the medicinal plant was collected from Palu of central Sulawesi and extracted with ethanol solvent with use of Six different concentrations (31.25 µg/ml, 62.5 µg/ml, 125 µg/ml, 250 µg/ml, 500 µg/ml and 1000 µg/ml) of leaf extracts were used to investigate study the in-vitro cytotoxicity concentration potential of the medicinal plant. The cytotoxicity potential of various extracts is N-Heksan extract of *Abelmoschus manihot* (L.) Medik with CTC_{50} values of *Abelmoschus manihot* (L.) Medik is displayed in **Table 3** and **Figure 2**. The results that the cytotoxicity rate has increased when the concentrations of leaf *Abelmoschus manihot* (L.) Medik extracts increases. MTT assay measured the viability cell based on the reduction of yellow tetrazolium MTT to a purple formazan dye by mitochondrial succinate dehydrogenase enzyme. Where the amount of formazan produced reflected the number of metabolically active 4 T1 cells Line (Breast Cancer). The test substances Leaf Extract (ethanol), Leaf Extract (ethyl acetate) and Leaf Extract (N-Heksan) were exhibited a CTC_{50} value of 261.84 ± 0.13 µg/ml, 288.29 ± 0.10 µg/ml and 185.06 ± 0.12 µg/ml. According to the criteria value of the cytotoxicity level of extracts, if an excerpt of natural ingredients with CTC_{50} < 100 µg/ml is very active, the CTC_{50} value of 100–200 µg/ml is quite active and > 200 µg/ml is weak [31]. The

NO	Name of Test Substance	Test Conc. (μg/ml)	% Cytotoxicity	CTC_{50} (μg/ml)
1	Leaf extract (Ethanol)	1000	*83.31 ± 0.003*	261.84 ± 0.13
		500	*73.44 ± 0.014*	
		250	*54.25 ± 0.025*	
		125	*19.93 ± 0.020*	
		62.5	*18.64 ± 0.066*	
		31.25	*2.56 ± 0.049*	
2	Leaf extract (Ethyl Acetate)	1000	66.28 ± 0.016	288.29 ± 0.10
		500	57.02 ± 0.007	
		250	54.45 ± 0.019	
		125	40.81 ± 0.025	
		62.5	28.17 ± 0.011	
		31.25	12.29 ± 0.020	
3	Leaf extract (N-Heksan)	1000	94.45 ± 0.006	185.06 ± 0.12
		500	67.77 ± 0.014	
		250	52.36 ± 0.038	
		125	37.50 ± 0.005	
		62.5	25.33 ± 0.015	
		31.25	16.55 ± 0.017	
4	Doxorubicin	100	68.24 ± 0.007	13.57 ± 0.10
		50	62.50 ± 0.007	
		25	53.51 ± 0.017	
		12.5	47.09 ± 0.109	
		6.25	42.29 ± 0.009	
		3.12	40.00 ± 0.002	

CTC_{50}- Cytotoxicity concentration.

Table 3.
Cytotoxic properties of test substances of leaf Abelmoschus Manihot *(L.) Medik on 4 T1 cell line [32].*

results of N-Heksan leaf extract *Abelmoschus manihot* (L.) Medik has quite potentially to the cytotoxicity. The N-Heksan leaf extract *Abelmoschus manihot* (L.) Medik shows the better percentage of growth inhibition CTC_{50} is 185.06 ± 0.12 μg/ml 4 T1 cell lines. To the Doxorubicin of cytotoxicity CTC_{50} with value 4 T1 cells line is 13,57 ± 0.10 μg/ml, where this value shows is toxic of Doxorubicin to 4 T1 cells Line (Breast Cancer). The cytotoxicity with various concentrations of all leaf extracts does not have potentially the cytotoxicity on Vero (normal) cell, where the cytotoxicity with value $CTC_{50} \geq 200$ μg/ml. The test substances Leaf Extract (ethanol), Leaf Extract (ethyl acetate) and Leaf Extract (N-Heksan), were exhibited a CTC_{50} value of 588.39 ± 0.13 μg/ml, 451.41 ± 0.11 μg/ml and 559.12 ± 0.13 μg/ml. According to the criteria value of the cytotoxicity level of extracts, if an extract of natural ingredients with $CTC_{50} < 100$ μg/ml is very active, the CTC_{50} value of 100–200 μg/ml is quite active and > 200 μg/ml is weak, where is displayed in **Table 4** and **Figure 3**. Results that the cytotoxicity rate has increased when the concentrations of leaf *Abelmoschus manihot* (L.) Medik extracts increases. To the Doxorubicin cytotoxic CTC_{50} value to Vero (normal) cells is 60.85 ± 0.13 μg/ml, this shows is toxic from according to the criteria

No	Name of Test Substance	Test Conc. (μg/ml)	% Cytotoxicity	CTC_{50} (μg/ml)
1	Leaf extract (Ethanol)	1000	57.98 ± 0.051	588.39 ± 0.13
		500	56.43 ± 0.062	
		250	23.33 ± 0.027	
		125	19.74 ± 0.006	
		62.5	9.29 ± 0.006	
		31.25	0.00 ± 0.038	
2	Leaf extract (Etil Acetat)	1000	65.34 ± 0.005	451.41 ± 0.11
		500	54.98 ± 0.003	
		250	38.52 ± 0.006	
		125	25.75 ± 0.002	
		62.5	9.39 ± 0.002	
		31.25	0.77 ± 0.006	
3	Leaf extract (N-Heksan)	1000	68.44 ± 0.005	559.12 ± 0.13
		500	37.07 ± 0.101	
		250	31.55 ± 0.004	
		125	26.42 ± 0.010	
		62.5	12.58 ± 0.056	
		31.25	0.00 ± 0.030	
4	Doxorubicin	100	99.71 ± 0.011	60.85 ± 0.13
		50	94.77 ± 0.005	
		25	84.60 ± 0.065	
		12.5	58.95 ± 0.057	
		6.25	52.95 ± 0.064	
		3.12	37.27 ± 0.008	

CTC_{50}- Cytotoxicity concentration.

Table 4.
Cytotoxic properties of test substances against on Vero cells [32].

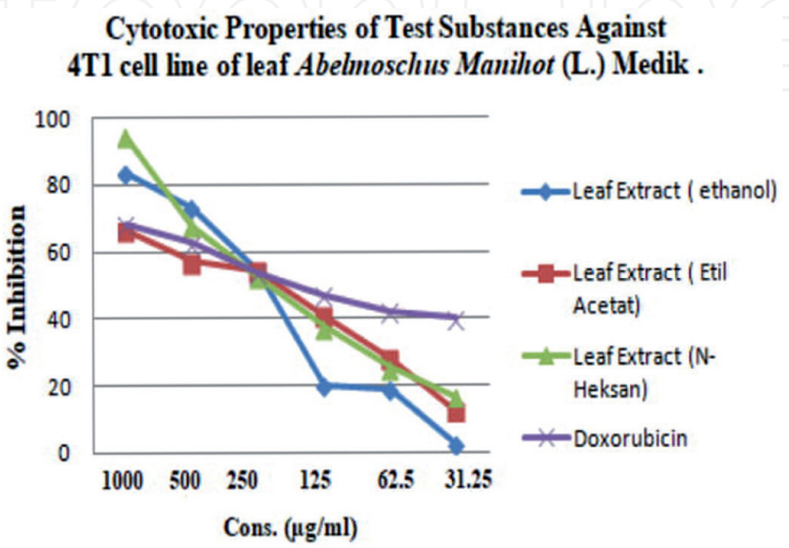

Figure 2.
Graph of cytotoxic effect on 4 T1 cells line of Abelmoschus Manihot *(L.) Medik [32].*

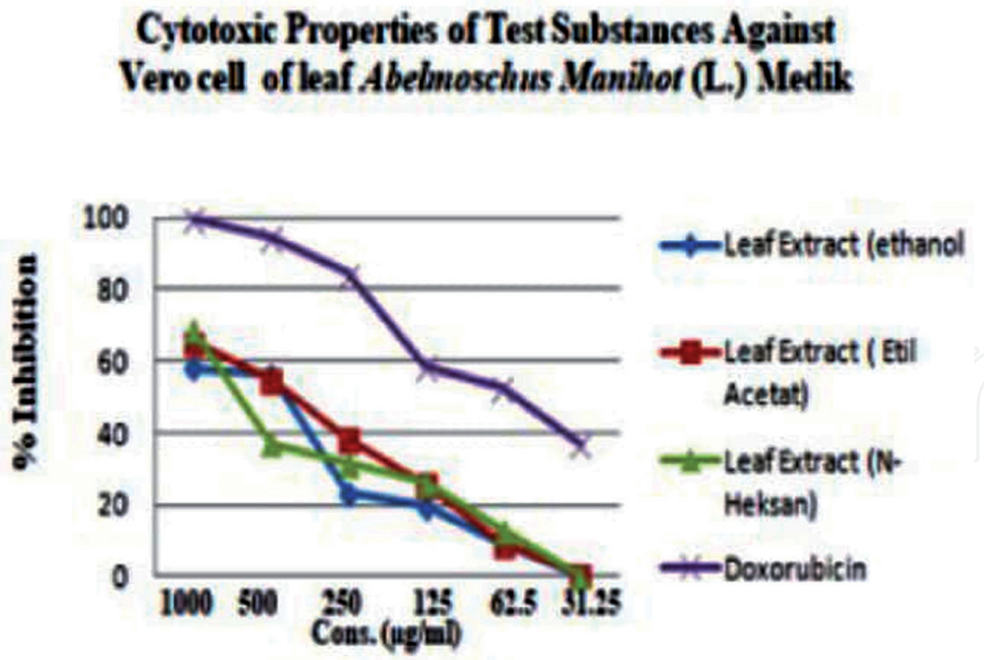

Figure 3.
Graph of the cytotoxic effect of Abelmoschus Manihot *(L.) Medik on Vero cell [32].*

value of cytotoxicity level [32]. The medicinal plant of leaf *Abelmoschus manihot* (L.) Medik from Palu of Central Sulawesi extract, where can be used to prepare the natural antioxidant and to prepare the pharmaceutical-based natural drug with proper standardization methods. Medicinal plants are a source of important therapeutic for alleviating human ailments and the medicinal plants have bioactive compounds, which are used for curing various human disease and also play an essential role key in chronic disease to especially on spinal muscular atrophy cell system pathway [33]. The natural antioxidant as a reduces the free radical of spinal muscular atrophy, stimulates the growth of normal cells, to protects the cell against the premature and abnormal aging condition of spinal muscular atrophy, helps fight the age-related molecular degeneration of spinal muscular atrophy and the last to supports the body immune system [34, 35].

10. Summary

The muscular atrophy recessive autosomal in neuromuscular with characterized of alpha motor neuron in the spinal cord, the neuromuscular disorders is one factor genetic of infant mortality and the spinal muscular atrophy deletion or mutation the Survival motor neuron. Spinal muscular atrophy is a defect in survival motor neuron 1 (SMN 1) and it's gene localized to 5q11.2-q13.3). SMN gene (SMN 1 and SMN 2) on chromosome 5q13 and the homozygous deletion of the SMN 1 gene result in Spinal muscular atrophy. The spinal muscular atrophy disease need of natural antioxidant as a reduces the free radical of the fiber muscle cell, stimulates the growth of normal cells, to protects the cell against the premature and abnormal aging condition of spinal muscle fiber, helps fight the age-related molecular degeneration of spinal muscular cell and the last to supports the body immune system. The medicinal plant of leaf *Abelmoschus Manihot* (L.) Medik from Palu of Central Sulawesi extract, where can be used to prepare the natural antioxidant and to prepare the pharmaceutical-based natural drug with proper standardization methods. Medicinal plants are a source of important therapeutic for alleviating

human ailments and medicinal plants have bioactive compounds, which are used for curing various human disease and also play an essential role key in chronic disease to especially on spinal muscular atrophy cell system pathway.

Acknowledgements

Especially Praise the father, praise the Son, praise the spirit three in one God of glory, Majesty praise forever to the King of King my lovely Jesus Christ. But He said to me, "My grace is sufficient for you, for my power is made perfect in weakness (2 Corinthians 12:9).

Conflict of interest

The authors have no conflict of interest.

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