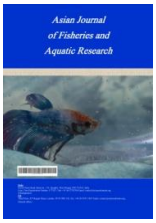

Asian Journal of Fisheries and Aquatic Research

10(2): 1-8, 2020; Article no.AJFAR.62754
ISSN: 2582-3760

A Mini-review: Effect of *Dunaliella salina* on the Growth and Health of Fish

Dian Yuni Pratiwi[1*]

[1]*Fisheries Department, Faculty of Fishery and Marine Science, Universitas Padjadjaran, Indonesia.*

Author's contribution

The sole author designed, analysed, interpreted and prepared the manuscript.

Article Information

DOI: 10.9734/AJFAR/2020/v10i230176
Editor(s):
(1) Dr. Emmanuel Tetteh-Doku Mensah, CSIR-Water Research Institute Aquaculture Research and Development Centre, Ghana.
Reviewers:
(1) Süleyman Çýlek, Kirikkale University, Turkey.
(2) Deniz Erguden, University of Iskenderun Technical, Turkey.
Complete Peer review History: http://www.sdiarticle4.com/review-history/62754

Mini-review Article

Received 02 September 2020
Accepted 09 November 2020
Published 27 November 2020

ABSTRACT

Fisheries is one of the sectors that can be developed to meet world food needs. The development of the fisheries is influenced by the availability of quality feeds. *Dunaliella salina* is a unicellular green algae that can be used as fish feeds. *D. salina* is known to contain many nutrients such as protein, carbohydrates, fats, pigments, and others. *D. salina* has also been shown to increase the growth rate of various types of fish. Not only for growth, but several studies have shown that *D. salina* has favorable effects on immunology. This article aims to explain the nutritional content and the effect of *D. salina* on the growth and health of fish. Based on the above studies, *D. salina* has the potential to be used as an alternative feed for various types of fish.

Keywords: Dunaliella salina; green algae; feed, growth, immunology.

1. INTRODUCTION

Fisheries is one of the sectors needed by the world community. The fisheries sector plays important roles as a source of nutritious food, a source of employment opportunities, and others. Fishery products are not only used for human consumption. Based on data in 2018, about 88% of fishery products are consumed by humans. While 12% is used for non-food purposes [1,2] such as pharmaceutical, cosmeceutical, nutraceutical applications, as biofuel production, and academic purposes [3].

**Corresponding author: Email: dianyunipratiwi@yahoo.com;*

Global fishery production shows an increase from year to year [2]. However, there are several challenges to maintaining the quality of fisheries products. The challenges are pathogens [4] and fish feed [5]. Bacterial infection can cause the death of fish. The bacteria that often infect fish are *Aeromonas complex, Pseudomonas fluorescens, Vibrio anguillarum, Mycobacterium fortuitum, Mycobacterium marinum, Edwardsiella ictaluri* [6], *Edwardsiella tarda* [4]. Several viruses that can infect fish are viral hemorrhagic septicemia virus [7], infectious haematopoietic necrosis virus, koi herpesvirus, epizootic haematopoietic necrosis virus, nervous necrosis virus, and others [8]. Fish diseases caused by bacteria or viruses can affect the amount of fish production and cause economic losses [9].

Antibiotics and vaccines have been used to overcome this problem. However, continuous antibiotics can make fish resistant to bacteria. The bacteria then can pass to human bodies.

Another obstacle is the limited number of vaccines that have been registered and marketed [10]. Therefore, the search and development of new materials that can be used as antibacterial, antiviral, and also have a good impact on fish growth needs to be done.

D. salina has been used as natural food. Some researchers have also proven that *D. salina* can increase the growth of several types of fish. Nutritional contents in *D. salina* such as beta carotene have also been shown to increase the immune system of fish [11]. This article aims to describe the nutritional content of *D. salina* and its effects on the growth and health of various types of fish.

2. CHEMICAL CONTENT OF *Dunaliella salina*

Dunaliella salina is a unicellular halophilic green algae. The flagellate microalgae, *D. salina* is highly responsive to osmotic changes permitting rapid changes in the cell color (green, orange, or red). This color change occurs because of the ability of *D. salina* to synthesize carotene [12]. *D. salina* has a thin elastic plasma membrane to protect its cells permitting rapid changes in the cell size. The optimum conditions for growth are high pH 8 [13], high salinities (45 PSU), low temperatures (20ºC), high light intensities (18x103 lux) [14].

Dunaliella salina has been widely used as natural food for fish because it contains a lot of nutrients. The nutritional contents of *D. salina* are protein, amino acids, carbohydrate, lipids, pigments, vitamins, minerals, antioxidants, and others. The amino acids contained include aspartic acid, glutamic acid, serine, histidine, glycine, lysine, leucine, isoleucine, phenylalanine, valine, methionine, tyrosine, alanine, arginine, threonine [15]. *D. salina* also contains saturated fatty acids (palmitic acid, stearic acid, myristic acid, margaric acid), monounsaturated fatty acids (Oleic acid, Arachidonic, erucic acid), and Polyunsaturated fatty acids (Linoleic acid, linolenic acid). The content of total saturated fatty acids, monounsaturated fatty acids, and polyunsaturated fatty acids, respectively, is 1532.68 mg / g, 567.50 mg / g, 1055.97 mg / g dry basis [16].

However, the nutritional content of *D. salina* can be influenced by the content in the growth media used. If the medium contains nitrogen, microalgae will use this nitrogen for protein and amino acid synthesis [17]. However, if nitrogen is low, algae tend to form lipids as food reserves compared to carbohydrates. The increase in carbohydrate content in algae can also be caused by limited phosphorus in the medium [18]. The content of macronutrients (protein, lipids, and carbohydrates) and amino acids in *D. salina* grown on different mediums can be seen in Table 1 and Table 2.

Dunaliella salina can photosynthesize with the pigments contained, namely lutein, chlorophyll a, chlorophyll b, β-Carotene, zeaxanthin and other.

Table 1. Effect of culture media on lipid, protein, and carbohydrate content in *D. salina* biomass *(reference)*

Medium	Lipid (%)	Carbohydrate (%)	Crude Protein (%)	Reference
Guillard's $F/_2$	31.3	19.1	5.6	[19]
Conway	43.3	23.4	6.9	[19]
Johnson	28.6	38.3	11.3	[19]
Waste Water tofu 81% + technical fertilizer 19%	0.063	15.07	17.08	[15]

The pigments content in *Dunaliella salina* can be affected by salinity. *Dunaliella salina* when experiencing abiotic stress such as high salinity will release secondary metabolites as a self-defense mechanism. This is what causes differences in the pigment content at different salinity. Apart from salinity, pigment content can also be different for each growth phase. In the exponential phase, *Dunaliella salina* will produce primary metabolites to survive. When entering the stationary phase, *Dunaliella salina* will produce more secondary metabolites such as chlorophyll and carotenoids as a self-defense response. However, slowly the pigment content will decrease in line with the number of cell death [21]. Table 3 shows the content of several pigments in *Dunaliella salina* cultivated at various salinities.

3. ANTIBACTERIAL AND ANTIVIRAL ACTIVITY OF *Dunaliella salina*

Bacterial and viral infections are obstacles in the world of fisheries. The development and discovery of substances that have antibacterial and antiviral activity need to be done. *D. salina* can synthesize various secondary metabolites that have potential as antibacterial and antiviral agents. Secondary metabolites found in *D. salina* are lutein [25], tannin, saponin flavonoids, alkaloids [3], chlorophyll a, chlorophyll b, ß-carotene [22], and so on.

Flavonoid can impairment of membrane functions, alteration of cytoplasmic membrane fluidity, inhibition of cell wall formation, inhibition of cell membrane formation, and interruption of synthesis of nucleic acid, inhibition of respiratory metabolism [26]. Terpenoids have antibacterial activity because they can cause membrane disruption [27]. Carotenoids are suggested to express lysozyme, which functions to digest bacterial cell walls [28].

Antiviral mechanisms by secondary metabolites are carried out by interacting wisth the extracellular viral particles and interacting with cell receptors to hindering viral entry [29]. Flavonoid inhibits the activity of viral enzyme (neuraminidases, DNA/RNA polymerases, and protease of virus [30]. The antiviral mechanism of terpenoids is inactivating virus-free particles [31]. Tannins can bind to capsid proteins, inhibit viral replication, and inhibit viral protein synthesis which is involved in the formation of new viral particles [32]. Beta carotene with the in silico approach demonstrated the ability to bind to viral capsid proteins [33].

Several studies have shown that *D. salina* can inhibit bacterial growth. This is thought to be due to the content of secondary metabolites in *D. salina*. Table 4 shows the ability of *D. salina* to inhibit the growth of some bacteria. *D. salina* also demonstrated antiviral activity against nervous necrosis virus, iridovirus, and white spot syndrome virus.

4. EFFECT OF *Dunaliella salina* ON GROWTH PERFORMANCE OF FISH

Research on *D. salina* as an alternative feed has been widely carried out. This algae has been shown to increase growth in rainbow trout (*Oncrohynchus mykiss*) [36], red tilapia (*Oreochromis spp.*) [37], *Dicentrarchus labrax* [38], and nile tilapia (Oreochromis niloticus) [39].

Table 2. Amino acids in *D. salina (reference)*

Amino acids	MH Medium (%) [20]	Waste Water tofu 81% + technical fertilizer 19% (%) [15]
Aspartic	13.3	0.73
Threonine	3.13	0.29
Serine	3.25	0.37
Glutamic	11.46	0.73
Glycine	12.76	0.39
Alanine	13.44	0.46
Valine	4.74	0.37
Isoleucine	2.56	0.29
Leucine	9.24	0.45
Tyrosine	2.42	0.21
Phenylalanine	3.58	0.32
Histidine	0.89	0.07
Lysine	4.70	0.25
Arginine	2.80	0.33

Table 3. Chlorophyll a, chlorophyll b, carotene b, and caratenoid content in *D. salina* at different salinity according to previous researches

Pigments	Salinity					
	20 ppt	25 ppt	30 ppt	35 ppt	40 ppt	Reference
chlorophyll a (mg/l)	9.232	9.900	10.961	9.046	8.873	[22]
Chlorophyll b (mg/l)	3.092	3.111	3.636	3.048	2.833	[22]
b-karotene (mg/l)	0.4845	-	2.3120	-	0.9520	[23]
Karotenoid (µg/ml)	0.25	-	0.67	-	0.95	[24]

Table 4. Antibacterial activity of *D. salina*

Bacterial strains	Extract	Inhibition zone (mm)	Reference
Escherichia coli	ethanol	11.33±0.52	[33]
Klebsiella pneumonia	ethanol	12.37±0.41	[33]
Staphlycoccus aureus	ethanol	8.73±0.12	[33]
Proteus vulgaris	ethanol	6.17±0.12	[33]
Lactococcus garvieae	ethanol	18.21±0.09	[34]
Yersinia ruckeri	ethanol	18.21±0.09	[34]
Vibrio anguillarum m1	ethanol	15.44±0.25	[34]
Salmonela enteritidis rskk 171	ethanol	15.28±0.12	[34]
Vibrio alginolyticus	hexane	16.92±0.53	[34]
Pseudomonas aeruginosa	hexane	10.90±0.21	[34]
Bacillus cereus s rskk 863	metanol	16.53±0.13	[35]
Pectobacterium carotovorum subsp. carotovorum dsm30168	ethanol	11.0 ± 0.1	[35]
Bacillus subtilis et-1	ethanol	21.0 ± 0.2	[35]
Edwardsiella tarda	hexane	20.07±0.19	[4]

Table 5. Effect of dietary *D. salina* on growth weight of Nile tilapia, red tilapia, and rainbow trout according to previous researches

Fish	*Dunaliella salina*	Initial Weight (g)	Final Weight (g)	Body Weight Gain (g)	Reference
Red Tilapia	200 mg/kg	3.04	13.14	10.10	[37]
	400 mg/kg	3.03	13.59	10.57	
	600 mg/kg	3.09	12.52	9.43	
Nile Tilapia	11 g/kg	44.00	70.63	26.63	[39]
Rainbow trout	5 g/kg	100	450	350	[36]
	7 g/kg	100	500	400	
	9 g/kg	100	526	426	
	11 g/kg	100	550	450	

Administration of 11 g/kg *D. salina* diet to nile tilapia can increase the weight of tilapia compared to control. The weight of initial tilapia before treatment was 44.00 g ± 0.58, after giving *D. salina* for 60 days it reached 70.63 g ± 0.41. Meanwhile, the weight of tilapia that was not given *D. salina* after 60 days only reached 63.57 ± 0.72 [39]. Supplementation of *D. salina* also increased the weight of red tilapia compared to control. The body weight gains of red tilapia that are given 200, 400, and 600 mg/kg diets *D. salina* are 10.10 g, 10.57 g, and 9.43 g, respectively. These values are higher than the control (8.00 g) [37]. Giving *D. salina* 5, 7, 9, and 11 g/kg diets to rainbow trout (*O. mykiss*) can also increase the bodyweight of fish, namely 450 g, 500 g, 526 g, and 550 g, respectively. Supplementation of *D. salina* can also increase the body length of *D. labrax* larvae cultured for 25 days [38].

The increase in fish weight can be caused by the nutritional contents found in *D. salina*. Lipids, carbohydrates, and proteins in *D. salina* not only for the basal metabolic needs of fish but are also effectively used for growth. *D. salina* is one of the algae species that contains high ß carotene. This pigment has been shown to increase the growth of Nile tilapia [39].

The provision of *D. salina* can also reduce the feed conversion ratio and increase the survival rate of red tilapia and nile tilapia. The feed conversion ratio for nile tilapia given 11 g/kg of *D. salina* was 36.37 at 1.37, while for control was 1.63. The feed conversion ratio for red tilapia given 200, 400, 600 mg/kg *D. salina* was 2.47, 2.36, 2.47 respectively, while the FCR in the control was 2.84. The lower feed conversion ratio indicates that the performance of feed supplemented with *D. salina* is better than the control. This can occur because of the high protein content in *D. salina*. The higher the protein content in the feed, the greater the amount of protein that can be used for growth so that the FCR value can be lower. The low FCR value also indicates that the total cost required for fish production is also low.

5. EFFECT OF *Dunaliella salina* ON HEALTH OF FISH

Several studies have proven that small amounts of *D. salina* in fish diets gives positive effects on health. Administration of 5 mg and 10 mg of lead acetate to nile tilapia caused the darkening of the fish skin, increased mucus secretion, and abnormal swimming. The mortality rates of nile tilapia given 5 mg and 10 mg of lead acetate were 13.3% and 22.2%, respectively. However, the mortality rates were decreased to 0.00% (5 mg lead acetate) and 4.45% (10 mg lead acetate) when the nile tilapia were given 11 mg/kg of *D. salina*. This is because ß carotene in *D. salina* acts as an antioxidant, thereby increasing the performance of serum antioxidant enzymes and reducing malondialdehyde. Malondialdehyde is a dialdehyde compound that shows the level of lipid peroxidase. Low malondialdehyde indicates that the lipid oxidation process in the cell membrane is low [39]. The results of this study are also in line with studies on red tilapia given 200, 400, and 600 mg/kg *D. salina*. The value of TBAR (index of lipid peroxidation and oxidative stress) in fish given *D. salina* was lower than that in control [37].

Viral nervous necrosis (VNN) is a virus that is a problem in the world of fisheries. One indicator of the virus infection is NFKB. NFKB (Nuclear Factor Kappa Beta) is a protein that controls the immune response to viruses. If VNN infects the fish body, the NFKB will be expressed and activate the immune response. *D. salina* has the potential to be developed as a VNN antiviral agent. NFKB levels in Grouper that was given 250, 300, 350 and 400 mg/kg *D. salina* compared to controls. Thus, it can be said that *D. salina* can act as a VNN antiviral [40].

The immunoglobulin (igM) content of rainbow trout which was given 5, 7, 9 and 11 grams of *D. salina* was increased compared to control. The result proves that *D. salina* can increase the body's immune response to rainbow trout [36].

6. CONCLUSION

In conclusion, *D. salina* gives a positive effect on the growth and health of fish. *D. salina can increase the weight of fish. D. salina* also has antibacterial and antiviral effect. So, this algae may be an excellent source to develop as a fish feed ingredient, antibacterial, and antivirus agent.

COMPETING INTERESTS

Author has declared that no competing interests exist.

REFERENCES

1. FAO. The state of world fisheries and aquaculture 2020. Sustainability in action. Rome; 2020. Accessed 15 October 2020.

Available:https://doi.org/10.4060/ca9229en

2. Dirican S, Musul H, Cilek S. Some physico-chemical characteristic and rotifers of camligoze Dam Lake, Susehri, Sivas, Turkey. Journal of Animal Veterinary Advances. 2009;8(4):715-719.
3. Leal MC, Rocha RJM, Rosa R, Calado R. Aquaculture of marine non-food organisms: What, why, and how? Reviews in Aquaculture. 2018;10(2):400-423.
4. Rusmawanto, Prajitno A, Yuniarti A. Minimum inhibitory concentration of marine microalgae *Dunaliella salina* on fish pathogenic bacteria Edwardsiella tarda. Research Journal of Life Science. 2019; 6(2):72-82.
   Available:https://doi.org/10.21776/ub.rjls.2019.006.02.1
5. Joseph I. Aquaculture feeds and feeding: Major challenges and issues. Conference: International workshop on status of good practices and lessons learnt in aquaculture in SAARC region. Cochin, India. 2013;271-276.
6. Guzman ED, Shotts EB, Gratzek JB. Review of bacterial diseases of aquarium fish. International association for aquatic animal medicine conference proceedings; 1986.
7. Escobar EL, Escobar-Dodero J, Phelps NBD. Infectious disease in fish: Global risk of viral hemorrhagicsepticemia virus. Reviews in Fish Biology and Fisheries. 2018;28(3).
   Available:https://doi.org/10.1007/s11160-018-9524-3 28(3)
8. Walker PJ, Winton JR. Emerging viral diseases of fish and shrimp. Veterinary Research. 2010;41(6):51.
   DOI: 10.1051/vetres/2010022
9. Tavares-Dias M, Martins ML. An overall estimation of losses caused by diseases in the Brazilian fish farms. Journal of Parasitic Diseases. 2017;41(4):913–918.
   DOI: 10.1007/s12639-017-0938-y
10. Kayansamruaj P, Areechon N, Unajak S. Development of fish vaccine in Southeast Asia: A challenge for the sustainability of SE Asia aquaculture. Fish and Shellfish Immunology. 2020;103:73-87.
11. Alishahi M, Karamifan M, Mesbah M, Zarei M. Hemato-Immunological responses of Heros severusfed diet supplemented with different levels of Dunaliella salina. Fish Physiology and Biochemistry. 2014;40:57-65.
    DOI: 10.1007/s10695-013-9823-5
12. Ramos AA, Polle J, Tran D, Cushman JC, Jin ES, Varela JC. The unicellular green alga dunaliella salina teod as a model for abiotic stress tolerance: Genetic advances and future perspectives. Algae. 2011; 26(1): 3-20.
    DOI: 10.4490/algae.2011.26.1.003
13. Dhaka P, Singh GP. Effect of pH on growth and biopigment accumulation of green alga *Dunaliella salina*. International Journal of Pharmaceutical Sciences and Research. 2018;9(1):271-276.
14. Abu-Rezq TS, Al-Hooti S, Jacob DA. Optimum culture conditions required for the locally isolated *Dunaliella salina*. Journal of Algal Biomass Utilization. 2010;1(2):12-19.
15. Darsi R, Supriadi A, Sasanti AD. Chemical characteristics and utilization potentials of *Dunaliella salina* and Nannochloropsis sp. Fishtech. 2012;1(1):14-25.
16. Molino A, Lovine A, Casella P, Mehariya S, Chianese S, Cerbone A et.al. Microalgae characterization for consolidated and new application in human food, animal feed and nutraceuticals. International Journal of Environmental Research and Public Health. 2018;15,2436.
    DOI:10.3390/ijerph15112436
17. Borowitzka MA, dan LJ. Borowitzka. Microalgal biotechnology. New York: Cambridge university press; 1988.
18. Markou G, Chatzpavlidis I, Georgakakis D. Effects of phosphorus concentration and light intensity on the biomass composition of *Arthrospira (Spirulina) platensis*. World Journal of Microbiology and Biotechnology. 2012;28:2661–2670.
19. Colussea GA, Mendes CRB, Duarte MER, De Carvalho JC, Noseda GAMD. Effects of different culture media on physiological features and laboratory scale production cost of *Dunaliella salina*. Biotechnology Reports. 2020;27(e00508).
20. Tammam AA, Fakhry EM, EL-Sheekh M. Effect of salt stress on antioxidant system and the metabolism of the reactive oxygen species in *Dunaliella salina* and *Dunaliella tertiolecta*. African Journal of Biotechnology. 2011;10(19):3795-3808
21. Sedjati S, Santosa GW, Yudiati E, Supriyantini E, Ridlo A, Kimberly FD.

Chlorophyll and carotenoid content of *Dunaliella salina* at various salinity stress and harvesting time. 4th international conference on tropical and coastal region eco development iop conf. series: Earth and Environmental Science. 2019;246.

22. Zainuddin M. Aktivitas antioksidan biopigmen *Dunaliella salina* pada media kultur hiposalin dan hipersalin, Indonesia. Jurnal Enggano. 2017;2(1):25-38.
23. Hermawan J. Peningkatan kandungan ß Karoten pada fitoplankton *Dunaliella salina* dengan media salinitas yang berbeda. Surabaya: Fakultas perikanan dan kelautan universitas airlangga; 2016.
24. Khairunnisa, Hasibuan S, Syafriadiman. The effect of different salinity on density and carotenoid content *Dunaliella salina* Jurnal Perikanan dan Kelautan; Indonesia. 2020;25(1):27-35.
25. Kimberly FD, Supriyantini E, Sedjati S. Growth and lutein content of *Dunaliella salina* at different salinity. Buletin Oseanografi Marina. 2019;8(1):44–48.
26. Naqvi SAR, Nadeem S, Komal S, Naqvi SAA, Mubarik MS, Qureshi SY et.al. Antioxidants: Natural antibiotics, 1st ed. London : IntechOpen; 2019.
27. Paiva PMG, Napoleão TH, Santos NDL, Correia MTS. Navarro DMAF, coelho LCBB. Plant compounds with *Aedes aegypti* larvicidal activity and other biological properties. M.-T. Liong (Ed.), Bioprocess sciences and technology. New York. Nova Science Publishers Inc; 2011.
28. Cucco M, Guasco B, Malacame G, Ottonelli R. Effects of β-carotene on adult immune condition and antibacterial activity in the eggs of the Grey Partridge (*Perdix perdix*). Comparative Biochemistry and Physiology, Part A 147. 2007;1038–1046.
29. Mendes GS, Soares AR, Martins FO, Maciel de Albuquerque MC, Costa SS, Yoneshigue-Valentin Y et.al. Antiviral activity of the green marine alga *Ulva fasciata* on the replication of human metapneumovirus. Rev. Inst. Med. trop. S. Paulo. 2010;52(1):3-10.
    Available: http://dx.doi.org/10.1590/S0036-46652010000100001.
30. Ninfali P, Antonelli A, Magnani M, Scarpa ES. Antiviral properties of flavonoids and delivery strategies. Nutrients. 2020;12(9): 2534.
    Doi:10.3390/nu12092534
31. Cox-Georgian D, Ramadoss N, Dona C, Basu C. Therapeutic and medicinal uses of terpenes. Medicinal Plants. 2019;333-359.
    DOI:10.1007/978-3-030-31269-5_15
32. Vilhelmova-Ilieva, N Galabov AS, Mileva M. Tannins as antiviral agents. Tannins-Structural Properties. Biological Properties and Current Knowledge; 2020.
    DOI:10.5772/intechopen.86490
33. Rubavathi S, Ramya M. Invitro assessment of antimicrobial and antioxidant activity of bioactive compounds from marine. International Journal of Current Microbiology and Applied Sciences. 2016;5(7):253-266.
34. Cakmak YS, Kaya M, Asan-Ozusaglami M. Biochemical composition and bioactivity creening of various extracts from Dunaliella salina, a green microalga. EXCLI Journal. 2014;13:679-690.
35. Ambrico A, Trupo M, Marelli R, Balducchi R, Ferraro A, Hristoforou E et.al. Effectiveness of *Dunaliella salina* extracts against bacillus subtilis and bacterial plant pathogens. Pathogens. 2020;9:613.
    DOI:10.3390/pathogens9080613
36. Amaninejad P, Emadi H, Ematiazjoo M, Sahhafi HH. Effects of *Dunaliella microalgae* (*Dunaliella salina*) on different level of IgM Immunoglobulin in rainbow trout (*Oncrohynchus mykiss*). Global Journal of Biodiversity Science And Management. 2013;3(2):237-242.
37. Arous WH, El-Bermawi NM, Shaltout OE, Essa MAE. Effect of adding different carotenoid sources on growth performance, pigmentation, stress response and quality in red tilapias (*Oreochromis* Spp). Middle East Journal of Applied Sciences. 2014;4(4):988-999.
38. Zaki MI, Saad H. Comparative study on growth and survival of larval and juvenile *Dicentrarchus labrax* rearing on rotifer and Artemia enriched with four different microalgae species. African Journal of Biotechnology. 2010;9(24):3676-3688.
39. Fadl SE, Habashi NE, Gad DM, Elkassas WM, Elbialy ZI, Abdelhady DH et al. Effect of adding dunaliella algae to fish diet on lead acetate toxicity and gene expression in the liver of Nile tilapia. Toxin reviews; 2019.
40. Yuwanita R, Yuniarti A, Rahardjo SSP, Ayu'nin Q, Madyaratri AM. The effect of

Dunaliella salina extract on NFkB expression in Cantang grouper (*Epinephelus fuscoguttatus* x *E. lanceolatus*) exposed by viral nervous necrosis. 2nd international conference on fisheries and marine science iop conf. series: Earth and Environmental Science. 2020; 441.
DOI:10.1088/1755-1315/441/1/012026

Peer-review history:
The peer review history for this paper can be accessed here:
http://www.sdiarticle4.com/review-history/62754