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NEW NON-TOXIC IRON CHELATOR SP10 CAN BE SUPPLEMENT AGAINST COVID-19

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ABSTRACT: *Based on the facts that non-toxic iron chelator SP10 and its homologues exhibit high anti-tumor, anti-bacterial, and anti-virus activity, we would like to propose that SP10 and its homologue can be Supplement against COVID-19, and another virus and unseen enemy which will appear in future.*
KEYWORDS: Iron chelator, Anti-tumor activity, anti-virus activity, COVID-19

INTRODUCTION

Iron is an essential element for all living organisms and plays an important role in critical cellular processes such as energy production, cell proliferation, and DNA synthesis. Although adequate iron levels are essential for human health, iron overload causes some disorders such as hemochromatosis, which is often referred as iron overload diseases (Nishida, 2012, 2015). In plasma of the patients with iron- overloading disorders, it is well known that the iron ion not associated with transferrin generally termed as non-transferrin-bound iron (NTBI), or labile plasma iron, is detected, and is present at concentration up to 10 μM (Evans et al, 2008; Hershko et al, 2005). The iron-overload causes carcinogenesis in some organs, and the oxidative stress due to the abnormally high levels of NTBI demonstrated in a number of neurodegenerative disorders including dementia, and Alzheimer's disease, is believed to be associated with neuronal death in these disorders (Nishida, 2004; Gaeta & Hider, 2005).

Thus, depletion of NTBI by an iron chelator has been explored as a possible therapeutic intervention in cancer and neurodegeneration (Nishida, 2012). In facts, some iron chelators have been shown to inhibit cancer cell proliferation, either alone (see Figure 1) or in combination with other anti-cancer drugs (Ohara et al, 2013; 2018). However, iron chelators can cause potentially serious side effects (Ohara et al., 2018). For example, deferasirox or *Exjade*, an oral iron chelator, has superior iron chelation ability, but cause digestive, liver, and kidney disorders. Deferoxamine (DFO) is an intravenous iron chelator that also exhibits toxic side effects. Decreasing the side effects of iron chelators

may improve cancer treatment compliance, thereby improving clinical outcomes

ANTI-TUMOR ACTIVITY OF NON-TOXIC IRON CHELATOR, SP10

Nishida has succeeded in synthesis of novel iron chelators named as Super-polyphenols (Nishida, 2012; 2015), which are shown to be non-toxic with reduced side effects, two examples of water-soluble super-polyphenols, SP9 and SP10, being illustrated in Figure 2 (Nishida, 2019). The non-toxicity of these compounds exemplified by Ohara et al. (Ohara et al, 2018) should be due to that these compounds cannot be a substrate for cytochrome P450 because of its hydrophilicity, and also to that the iron (III)-chelates of these super polyphenols are non-toxic, which is strongly supported by the studies on the chemical mechanism of the toxicity induced by the iron (III) with artificial chelates in human body done by Nishida (Nishida, 2019). The most important point is that these two chelates do not form a dangerous μ-oxo bridged dimeric iron (III) species, which has been pointed out to be main species to induce iron toxicity by NTBI (Nishida, 2012).

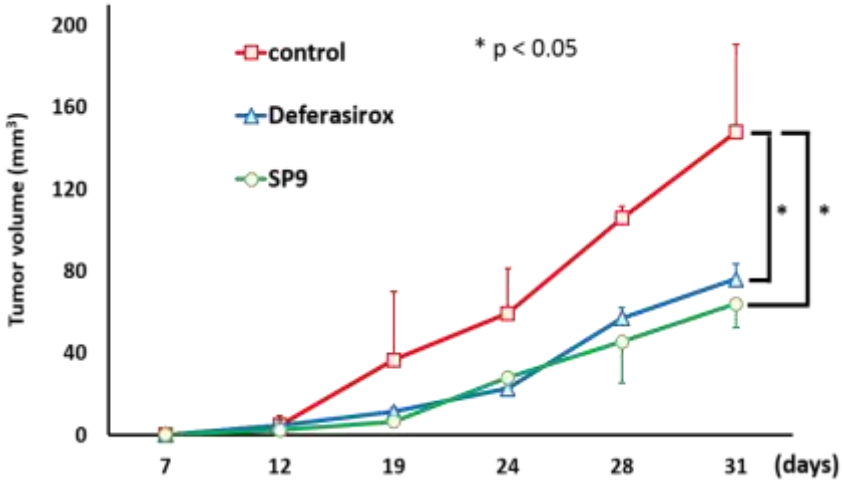
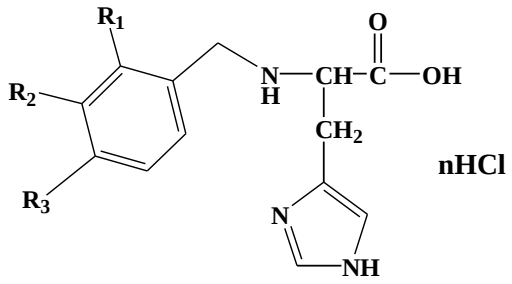


Figure 1. Anti-tumor effects of SP9 and Deferoshirax (Exjade) in an A549 tumor xenograft model (Nishida et al, 2018). Human A549 cells (3 x 10^6/mouse) was implanted subcutaneously into the nude mouse (BALB/c nu/nu, 6 weeks old) (Ohara et al. 2018), and treatment commenced 7 days after tumor injection. SP9 and Deferoshirax (Exjade) (20mg/Kg orally, given 5 days/week) effectively inhibited the growth of A549 allografts *in vivo* (*$p < 0.05$).

Ohara et al. have reported that SP10 inhibited cancer cell proliferation by inducing apoptosis in HCT116, HSC-2, A549, and MCF-7 cancer cells *in vitro* (Ohara et al, 2018),

and that SP10 and SP9 are shown to inhibit tumor growth in an HCT116 and A549 xenograft models *in vivo*, respectively (see Figure 1). Very recently Prof. Baba at Kagoshima University has observed that SP10 inhibited cancer cell proliferation of leukemia including MOLT-4, SIT, MT-2 and Hut-102 *in vitro* (Baba, 2016). The anti-tumor ability observed for SP10 may be attributed to that SP10 binds with Fe(III) ion in NTBI, changing the chemical nature of the iron(III) ion; especially preventing the transfer of iron(III) ion from NTBI to apo-transferrin (Nishida et al, 2007).



SP9: R_1=H, R_2=COOH, R_3=OH

SP10: R_1=OH, R_2=OH, R_3=OH

Figure 2. Chemical structures of SP9 (n=1) and SP10 (n=2) (Nishida, 2019)

ANTI-VIRUS and ANTI-BACTERIAL ACTIVITY OF SP10

In addition to above facts, Ohara et al. also observed that SP10 can depress the infection by human influenza virus PR8 (Nishida et al. 2018), and its homologues exhibit high anti-bacterial function towards *Streptococcus mutans* ATCC 25175 (SM) and *Aggregatibacter actinomycescomitans* Y4 (Aa), strongly inhibiting the proliferation of these bacteria (Nishida et al, 2018). All these facts are suggesting that SP10 and its homologues control the chemical properties of NTBI, inhibiting the growth of influenza virus and bacteria. These imply that SP10 and its homologues can be Supplement against COVID-19, and another virus and unseen enemy which will appear in future.

REFERENCES

Baba M. (2016): unpublished results.

Evans, R.W., Rafique, R., Zarea, A., Rapisarda, C., Cammack, R., Evans, P.J., Porter, J.B. and Hider, R.C. (2008): Nature of non-transferrin-bound iron: studies on iron

citrate complexes and thalassemia sera. J. Biol. Inorg. Chem. **13**, 57-74. doi:10.1007/s00775- 007-0297-8

Hershko, C., Link, G., Konjin, A. and Cabantchik, Z. I. (2005): Objective and mechanism of iron chelation therapy. Ann. N. Y. Acad. Sci. **1054**, 124-135. Doi:10.1196/annals.1345.015.

Gaeta, A. and Hider R.C. (2005): The crucial role of metal ions in neurodegeneration: the basis for a promising therapeutic strategy. Brit. J. Pharmacology. **146**, 1041-1059. doi:10.1038/sj.bip.0706416.

Nishida Y. (2004): Oxidative stress and neurodegeneration. Med. Hypothesis Res, **1**, 227-245. http://www.journal-mhr.com/PDF_Files/vol_1_4/1_4PDFs/1_4 _2.pdf

Nishida, Y., Ito, Y, & Satoh, T. (2007): Origin of the proximal renal injuries by Fe(III)-nta chelate. Z. Naturfortsh. **62c**, 608-612.

Nishida Y. (2012): The chemical mechanism of oxidative stress due to non-transferrin-bound iron (NTBI). .Adv. Biosci. Biotech., **3**, 1076-1086. doi:10.4236/abb.2012.327131.

Nishida Y. (2015): Iron chelators for labile iron removal therapy and enhancement of longevity. Eur. J. Biol. Med. Sci. Res. **3**, 42-51.

Nishida Y., Ohara T., Tomono Y. and Omori K. (2018): WO/2018/207852.

Nishida Y. (2019): New Non-toxic iron chelators SP9 and SP10, and its Potentiality as supplement for brain supplement.

https://brainsupplementoff/wixsite.com/mysite/journal.

Ohara T., Noma K., Urano S., Watanabe S., Nishitani S., Tomono Y., Kimura F., Kagawa S., Shirakawa Y., Fujiwara T. (2013): A novel synergistic effect of iron depletion on antiangiogenic cancer therapy. Int. J. Cancer, **132**, 2705-2713.

Ohara, T., Tomono, Y., Boyi X., Omori, K and Matsukawa A. (2018): A novel nontoxic iron chelator, super-polyphenol, effectively induces apoptosis in human cancer cell lines. Oncotarget, **9**, 32751-32760. Available on line at: www.oncotarget.com.