# A Yagi<sup>1\*</sup>, M Hasegawa<sup>2</sup>, M Mikami<sup>3</sup> and Kosuke Shiba<sup>4</sup>

<sup>1</sup>Special Advisor of Japan Aloe Science Association; Professor Emeritus of Fukuyama University, Hiroshima, Japan <sup>2</sup>Pharmacist, Kampo Pharmacy Grace-Meg-Salon, Toshima, Tokyo, Japan <sup>3</sup>A Former Nursing Officer, Japan Aloe Science Association Lecturer, Sapporo, Hokkaido, Japan <sup>4</sup>A Clinical Director of Medical Association and Occupational Physician, Yokohama-city, Kanagawa, Japan

\*Corresponding Author: A Yagi, Special Advisor of Japan Aloe Science Association; Professor Emeritus of Fukuyama University, Hiroshima, Japan.

Received: February 24, 2024; Published: April 05, 2024

# Abstract

In case report 1-2 (previous review article), we expressed children-growth supported with Aloe vera juice (AVJ) ingestion. Case report 3 and 4 (present review article): A 10-years old male who had 145 cm height, 55 kg body weight and Rhorer index 180.4, suffered from allergy and constipation. He consulted Kampo-pharmacy and started to ingest AVJ 100 ml/d. After 4-years ingestion, he has a happy school days without suffering from allergy and has Rhorer index 122.07 and a balanced diet and freely communications with his friends. A baby, diagnosed as Kawasaki's disease, had several drugs, and then suffered from a side effect with constipation. He ingested aloe vera juice 10 ml/d with slowly and carefully. After the ingestion of AVJ for several months, he had a nice QOL without constipation.

Keywords: Aloe Vera Gel Juice Ingestion; Obesity; Autism Child; Kawasaki's Disease

# Introduction

One in 68 U.S. children (1.47%) are believed to have autism or a related disorder, according to the Centers for diseuse control and prevention estimate. This is a 30% jump from the 2012 federal estimate. Many treatments to have been proposed for autism spectrum disorders (ASD) with the most effective being combined treatments involving specialized and supportive educational programming, communication training (e.g. speech/language therapy), social skills support and behavioral intervention. Nutrient power brings a unique to perspective to mental, behavioral and autism disorders including the crucial role of epigenetics [1]. Saito., *et al.* [2] estimated the prevalence and cumulative incidence of ASD annually, to determine whether there is a true increase in ASD prevalence by estimating the cumulative incidence of ASD annually, and to examine the rates of co-existing neuro-developmental disorders (NDD). In the cross-sectional sequential design study, all-5-years old children in the catchment in the underwent the screening annually from the year 2013 - 2016 were demonstrated in Japan. Screen-positive children were invited to participate in a comprehensive assessment, including child and

02

parent interview, behavioral observation, and cognitive and motor function testing. Adjusted ASD prevalence was 3.22%. The cumulative incidence of ASD up to 5 years of age for the total study years was 1.31%. Only 11.5% of children had ASD alone; the remaining 88.5% were found to have at least one co-existing NDD. Zuffa., et al. [3] revealed distinct gut microbial and metabolic development profiles of typically developing infants with and without family history of ASD during the first 3 years of life. And the differences were more pronounced at 5 months of age and characterized by lower abundance of *Clostridium* related species and GABA and by an increased abundance of *Clostridium* related species and butyrate in fecal samples of infants at elevated like-hood of ASD. Grimaldi., et al. [4] the effect of exclusion diets and prebiotics has been evaluated in autism, showing potential beneficial effects, A combined dietary approach resulted in significant changes in gut microbiota composition and metabolism suggesting that multiple interventions might be more relevant for the improvement of these aspects as well as psychological traits. Rose., et al. [5] have developed a lymphoblastoid cell line (LCL) model of autism spectrum disorders (ASD) with a subset of LCLs demonstrating mitochondrial dysfunction (AD-A) and another subset of LCLs demonstrating normal mitochondrial function (AD-N). Given the positive modulation of butyrate on mitochondrial function, the author hypothesized that butyrate would have a preferential positive effect of AD-A LCLs. To this end, the author measured mitochondrial function in ASD and age-matched control LCLs, all derived from boys following 24 and 48h exposure to butyrate (0, 0.1, 0.5 and 1 mM) both with and without an in vitro increase in reactive oxygen species. The data showed that the enteric microbiome-derived butyrate modulates mitochondrial activity, with this modulation dependent on concentration, microenvironment redox state, and the underlying mitochondrial function of the cells.

Present review article presents case report (previous case reports) 1-2 of children growth with ASD supported with Aloe vera juice long time ingestion. In case report-3: A 10-years old male who had Rhorer index 180.4, suffered from allergy and constipation, started to digest AVJ 100 ml/d on 2019. After 4-years ingestion he has a happy school days without suffering from allergy and had Rhorer index 122.07 and a balanced diet and freely communications with his friends. In case report-4, a baby diagnosed as Kawasaki's disease, had several drugs, and suffered from a side effect with constipation. He ingested AVJ 10 ml/d. with slowly and carefully. After the ingestion of AVJ for several months, he had a nice QOL without constipation.

# Obesity is the major predisposing factor to comorbidities; including type 2 diabetes, cardiovascular diseases, dyslipidemia and autism spectrum disease

Increasing evidence suggest a pivotal role played by alterations of gut microbiota (GM) that could represent the causative link between environmental factors and onset of obesity. Coppola., *et al.* [6] expressed that the beneficial effects of GM are mainly mediated by the secretion of various metabolites among which short chain fatty acid (SCFAs) produced by fermentation of dietary fibers and resistant starch with vast beneficial effects in energy metabolism, intestinal homeostasis and immune response regulation. Among SCFAs, butyrate emerged the preclinical and clinical data that contribute to explain the role of butyrate, highlighting its crucial contribute in the diet-GMhost health axis.

#### Long-term benefit of microbiota transfer therapy on autism syndromes and gut microbiota

Modifying the gut microbiome is a potential route to improve gastrointestinal (GI) and behavioral symptoms in children with autism spectrum disorders (ASD), and fecal microbiota transplant could transform the dysbiotic gut microbiome towards a healthy one by delivering a large number of commensal microbes from a healthy donor. Kang, *et al.* [7] reported on a follow-up with the 18 ASD-related symptoms-children two years after treatment was completed. Important changes in gut microbiota at the end of treatment remained at follow-up, including significant increase in bacterial diversity and relative abundances of *Bifidobacterium* and *Prevotella*. The author demonstrated the long-term safety and efficacy of microbiota transfer therapy as a potential to therapy to treat children with ASD who have GI problems.

03

#### Autism spectrum disorder is strongly associated with dysbiosis in gut microbiome

Zhang., *et al.* [8] proposed a novel analytic strategy: quasi-paired cohort, and applied it to a metagenomic study of the ASD comparing paired samples of ASD microbiome. By comparing paired samples of ASD and neurotypical subjects, the authors have identified significant deficiencies in ASD children in detoxifying enzymes and pathways, which show strong correlation biomarkers of mitochondrial dysfunction. Diagnostic models based on these detoxifying curate distinguished ASD individuals from controls, and the dysfunction score of ASD.

#### A new drug, semaglutide could spell an end to the world obesity epidemic

Semaglutide, trade name Wegovy, manufactured by Norvo Nordisk, Danish pharmaceutical company, is an antidiabetic medication used for treatment of type-2 diabetic medication and an anti-obesity medication with subcutaneous injection used for long-term weight management. It is a peptide similar to the hormone glucagon (GLP-1 receptor-like drug) and works like the body's own hormone to regulate the blood sugar(glucose) level and appetite. Wegovy started to use for an anti-obesity medication in Japan on Feb. 22, 2024 [9].

#### Possible hypoglycemic effect of Aloe vera high molecular weight fractions on type-2 diabetic patients

Aloe vera high molecular weight fraction (AHM) containing less that 10 ppm barbaloin and polysaccharide (MW: 10,000KD) with glycoprotein (verectin: MW 29KD), were prepared by patented hyper-dry system in combination of freeze-dry technique with microwave and far infra-red radiation. AHM produced significant decreased in blood glucose level sustained for 6 weeks of the start of the study. Significant decrease in triglycerides was only observed 4 weeks after treatment and continued thereafter. No deteriorate effects on kidney and liver functions were apparent. Oral administration of 9 male and 6 female out-diabetic-patients with AHM may relief vascular complications probably via activation of immune-system [10].

#### **Case Reports**

#### Case reports 1 - 2 [11], case report-3, and case report-4 in Kawasaki's disease baby

**Case report 1:** A 9-years old female born in April 2013 and Rhorer index 186.6 suffered from atopic dermatitis. She started to drink Aloe vera juice (AVJ) 50 ml/d on Apr. 2013 with taking a balance diet and the Rhorer index reduced 139.1 on October 2013. She continued to drink AVJ 50 ml/d and had no constipation and atopic dermatitis. On 23-years old, she had Rhorer index 134 and no atopic dermatitis with AVJ ingestion 100 ml/d and well-being on December 2022.

**Case report 2:** A 12-years-old female born in June 2010 and Rhorer index 170.9 had grown over fat. After then, she become a nonattender student on June, 2015. Since then, she started to drink AVJ 100 ml/d and Rhorer index 138.1. She started her first menstrual period and had a well-being QOL. In 23-years-old she continued to drink AVJ 100 ml/d with her exercise and kept her height 160 cm and body weight ~50 kg with her well-being on December 2022.

**Case report 3:** A 10-years-old male who had 145 cm heigh, 55 kg body weight and Rhorer index (w/h3x10) 180.4, suffered from allergy and constipation. He has an unbalanced diet, and eat bread, rice meet but does not eat vegetables and fishes. He can't communicate and repeats same words. On 10 years-old in September, 2019, he consulted to Kampo-Pharmacy and start to digest Aloe vera juice (AVJ) 10 ml/d slowly with a syringe. On December he had his heigh 147 cm and body weight 50 kg and he can understand his teacher's notice. On April 2020, he digested AVJ 50 ml/d and had Rhorer index 136.68 (Standard: ~130 kg/m<sup>3</sup>). He had a balanced diet and freely communicate with his friends. On August, 2023 his Rhorer index showed 122.07 with his 180 cm heigh and 50 kg weight, digesting AVJ 100 ml/d and has a happy school day without suffering from allergy.

**Case report 4:** ~One-year-baby, diagnosed as Kawasaki's disease, had several drugs, and then suffered from a side effect with constipation. Then, he ingested only AVJ 10 ml/d slowly and carefully, and after 6-months he had a nice QOL without constipation.

04

### **Discussion and Summary**

In previous article we focused on butyrate fermented in Aloe vera gel to obesity-prone and pediatric subjects [11] and a possible benefit of butyrate to obesity-prone children in long time digestion may participate to the children growth. It was demonstrated that nutrient power brings a unique perspective to mental, behavioral, and autistic disorders, with AVJ ingestion. In individuals with autism spectrum disorders (ASD), butyrate deficiency is likely a central cause of elevated inflammatory response in the gastrointestinal tract. Thus, supplementing the gut with additional butyrate and AVJ ingestion help it to make up for any native shortages, while also reducing the inflammatory responses created by other causes associated with ASD. Advanced treatments for mental illness will benefit greatly from daily long time AVJ ingestion and balanced diet in homeostasis [12]. An obesity often leads to all kinds of disease and is a root cause of many diseases specially in children growth. Mitigation of constipation- and ASD-children was exhibited in our Aloe vera factbook vol.3 from 196 AVJ-ingestion subjects in Japanese on January 1<sup>st</sup> 2024 [13].

# Acknowledgement

The authors express our deep appreciation for Mr. A. Mukaitani, Chairperson of Japan Aloe Science Association.

# **Bibliography**

- 1. Walsh WJ. "Nutrient Power: Heal your biochemistry and heal your brain". Skyhorse Publishing (2014).
- 2. Saito A., *et al.* "Prevalence and cumulative incidence of autism spectrum disorders and the patterns of co-occurring neurodevelopmental; disorders in a total population sample of 5-year-old children". *Molecular Autism* 11.1 (2020): 25.
- 3. Zuffa S., *et al.* "Early-life differences in the gut microbiota composition and functionality of infants at elevated likelihood of developing autism spectrum disorder". *Translational Psychiatry* 13 (2023): 257.
- 4. Grimaldi R., et al. "A prebiotic intervention study in children with autism spectrum disorders". Microbiome 6.1 (2018): 133.
- 5. Rose D., *et al.* "Butyrate enhances mitochondrial function during oxidative stress in cell lines from boys with autism". *Translational Psychiatry* 8.1 (2018): 42.
- 6. Coppola S., et al. "The protective role of butyrate against obesity and obesity-related diseases". Molecules 26.3 (2021): 682.
- 7. Kang DW., *et al.* "Long-term benefit of microbiota transfer therapy on autism symptoms and gut microbiota". *Science Reports* 9 (2019): 5821.
- 8. Zhang M., *et al.* "A quasi-paired cohort strategy reveals the impaired detoxifying function of microbes in the gut autistic children". *Science Advances* 6.43 (2020): eaba3760.
- 9. A Yagi., *et al.* "Prophylactic role of butyrate fermented in Aloe vera gel to typr-2 diabetic patients and obesity subjects: Case reports of obesity-prone individuals". *EC Clinical and Medical Case Reports* 6.1 (2023): 72-77.
- 10. A Yagi., *et al.* "Possible hypoglycemic effect of Aloe vera L. high molecular weight fractions on type-2 diabetic patients". *Saudi Pharmaceutical Journal* 17.3-4 (2009): 209-215.
- 11. Yagi A., *et al.* "Prophylactic efficacy of butyrate fermented in Aloe vera gel to obesity-prone subjects Case reports: Children-growth supported with Aloe vera juice ingestion". *EC Clinical and Case Reports* 6.3 (2023): 58-64.

- 05
- 12. Yagi A., *et al.* "Epigenetic roles of short chain fatty acids beneficial modulators in the neuroendocrine systems Case reports: Influence of Aloe vera juice to brain homeostasis". *Journal of Gastroenterology and Hepatology Research* 10.5 (2021): 3571-3579.
- 13. Aloe vera factbook volume 3 January 1<sup>st</sup> 2024, Supervised by Yagi A, and Publisher, Mukaitani A. Chairperson of Japan Aloe Science Association.

Volume 7 Issue 4 April 2024 ©All rights reserved by A Yagi., *et al.*