

Association of Butyrate Fermented in Aloe vera gel with α -Synuclein-induced DNA and Histone Damages in Parkinson's Disease Patients. Case reports: Remission of PD Patients with Diabetes, Drug-induced Parkinsonism, and Irritable Bowel Syndrome with Aloe vera gel Juice Ingestion

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ABSTRACT

α -Synuclein misfolding and aggregation are linked to the Parkinson's disease (PD) pathology. PD may begin with the intestinal accumulation of α -Syn fibrils, which can be casually associated with gut dysbiosis. The variability of gut microbiota across countries prevented us from identifying shared gut dysbiosis in PD. The intestinal mucin layer-degrading *Akkermanisia* is increased and

short chain fatty acids-producing *Roseburia* and *Faecaibayerium* are decreased in PD across countries. We discussed the relevance of gut microbiota, short chain fatty acids, butyrate, and gut dysbiosis in PD in disease progression. In case reports, remission of PD patients with diabetes and drug-induced Parkinsonism and irritable bowel syndrome with drug and aloe vera juice supplements as an adjuvant were exhibited.

Key words: Fermented butyrate in Aloe vera gel; Alpha-syn-induced DNA; Histone damage in PD patients

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INTRODUCTION

α -Synuclein (α -Syn) is generally assumed to be simply a presynaptic protein that forms abnormal cytoplasmic aggregates in Parkinson's disease (PD). This suggests that alterations in normal protein homeostasis may contribute to pathogenesis. α -Syn is a small, 140 amino acid protein that localizes to presynaptic terminals, where it regulates neurotransmitter vesicle cycling. Under pathological conditions α -Syn aggregates into somatic and neuritic inclusions. This aggregation occurs in neurons in PD. Evidence based on studies using in vitro and in vivo models, suggests that α -Syn nuclear regulates a number of nuclear functions, interacting directly with DNA and histone, in turn regulating gene transcription and also DNA repair. α -Syn misfolding and aggregation linked to the PD pathology. In the unbound form, α -Syn is a typical intrinsically disordered protein and

it can adopt different conformations depending on the environmental modulators. Many environmental factors promote α -Syn misfolding and aggregation^[1]. Rane *et al*^[2] explored executive function deficits in a rat model of PD in the pre-motor deficit stage. The rats were lesioned with 12 μ g of 6-hydroxydopamine (6-OHDO) in the stratum in two step processes (10 μ g/ μ l followed by 2 μ g/ μ l) 48 hours apart. The results demonstrated that performance by the pre-motor rat model of PD was equivalent to that of the control groups in the simple and the compound discriminations as well as the intradimensional set-shifting. However the PD group exhibited attention set-shifting deficits similar to those observed PD patients. Sodium butyrate (SB), a short chain fatty acid derivative and inhibitor of class I and II histone deacetylase, was tested as a potential therapeutic agent to mitigate the pre-motor cognitive deficits in PD. The SB treatment not only effectively alleviated the set-shifting deficits, but also improved the attentional set formation in the treated rats. Sharma *et al*^[3] investigated the effect of SB in 6-OHDA-induced experimental PD like symptoms in rat model. 6-OHDA treated rats showed elevated oxidative stress and neuro-inflammatory markers. Treatment with SB resulted in significant attenuation of motor deficits and increased striatal dopamine level. Moreover, SB treatment attenuated the oxidative stress and neuro-inflammatory markers. These effects occur concurrently with increased global H3 histone acetylation and brain derived neurotrophic factor levels. Thus, the author exhibited that the results of the study are indicative for the therapeutic potential of histone deacetylase (HDAC) inhibitors in PD. Laurent *et al*^[4] investigated the effects of SB on locomotor impairment and early mortality in a rotenone-induced PD model. The treatment with 10 mM SB-supplemented food rescued the rotenone-induced locomotor impairment and early mortality in flies, *Drosophila* transgenic model. The SB-mediated improvement of rotenone-induced locomotor impairment was associated with elevated dopamine level in the brain. The findings demonstrated that HDAC inhibitor, SB can ameliorate locomotor impairment in a rotenone-induced PD model. Paiva *et al*^[5] evaluated the impact of wild-type (WT) and mutant A30P α -Syn on gene expression, in a dopaminergic neuronal cell model, and decipher potential mechanisms underlying α -Syn-mediated transcriptional deregulation. The author performed gene expression analysis using RNA-sequencing in Lund Human Mesencephalic cells expressing endogenous (control) or increased level of WT or mutant A30P α -Syn. In dopaminergic neuronal cells, increased α -Syn expression led to the reduced levels of acetylated histone 3, importantly, treatment with SB, rescued WT α -Syn-induced DNA damage, possibly via upregulation of genes involved in DNA repair. The findings provided novel and compelling insight into the mechanisms associated with α -Syn neurotoxicity in dopaminergic cells, which could be ameliorated with an HDAC inhibitor, sodium butyrate.

Present review describes the beneficial efficacy of fermented butyrate in Aloe vera gel to Parkinson disease patients. In case reports, remission of PD patients with diabetes, the drug-induced Parkinsonism patient and the irritable bowel syndrome-patients together with Aloe vera juice supplement as an adjuvant was exhibited.

THE INTERACTION AT BLOOD-BRAIN BARRIERS OF MICROBIOME WITH THE CNS BARRIERS

The microbiome interacts with the central nervous system (CNS) and can regulate many of its functions. One mechanism for this interaction is at the level of the blood-brain barriers (BBBs). Metabolic

products produced by the microbiome, such as short chain fatty acids, can cross over the BBBs to affect brain function. Logsdon *et al*^[6] examined the several ways the microbiome is known to interact with the CNS barriers. Bacteria can directly release factors into the systemic circulation or can translocate into blood. Once in the blood, the microbiome and its factors can alter peripheral immune cells to promote interactions with the BBB and ultimately with other elements of the neurovascular unit. Bacteria and their factors or cytokines and other immune-active substances released from peripheral sites under the influence of the microbiome can cross the BBB, alter BBB integrity, change BBB transport rates, or induce release of neuro-immune substances from the barrier cells. Metabolic products produced by the microbiome, such as short chain fatty acids, can cross the BBB to affect brain function. Host immune systems are influenced by changes to the microbiota and offers new treatment strategies for CNS disease. The intestine also contains a barrier, and bacterial factors can translocate to the blood and interact with host immune cells. The metastatic bacteria factors can signal T-cell to become more CNS penetrant, thus providing a novel intervention for treating CNS disease.

THE IDENTITY OF AN ANTI-INFLAMMATORY ROLE OF SODIUM BUTYRATE FROM THE ASPECT OF MICROGLIAL PROCESS ELONGATION

Microglia, a type of immune cell in the brain, is in a ramified status with branched processes in normal conditions. Upon pathological stimulation, microglia retracts their processes and become activated. Wang *et al*^[7] investigated the influence of butyrate produced by fermentation of dietary fiber in the gut on microglial process. The protein kinase B (Akt)-RhoGTPase signal was considered to mediate the effect of SB on microglial process, as (1) SB activated the small RhoGTPases Rac1 and Cdc42; (2) SB promotes Akt phosphorylation; (3) Rac1, Cdc42, and Akt inhibition abrogated the pro-elongation effect of SB on microglial process. Akt inhibition prevented the anti-inflammatory effect of SB in primary cultured microglia, and abrogated the inhibitory effects of SB on microglial process retraction and behavioral abnormalities induced by lipopolysaccharide.

THE EFFECT OF SODIUM BUTYRATE ON GENE INFORMATION IN HIPPOCAMPAL MICROGLIA UNDER NEURO-INFLAMMATORY CONDITION

Chronic psychological stress increases pro-inflammatory cytokines and promotes microglial activation, leading to stress vulnerability. Epigenetics, including DNA methylation and histone modification, are related to the pathophysiology of major depressive disorder. Sodium butyrate (SB) exerts an anti-depressant effect by altering gene expression in the hippocampus. Yamawaki *et al*^[8] investigated whether lipopolysaccharide (LPS)-induced depressive-like behaviors in mice are affected by the repeated treatment with SB. Intraperitoneal injection of LPS (5 mg/kg) induced cytokines and ionized calcium-binding adaptor molecule 1, a marker of microglial activation, in the hippocampus. The results indicated 64 overlapping gene, between LPS-increased genes and SB-decreased genes. Among these genes, EF hand calcium binding domain 1 was a particularly distinct candidate gene. The findings indicated that microglial activation mediated through epigenetic regulation may be involved in depressive-like behaviors.

PROTECTIVE EFFECT OF SODIUM BUTYRATE AGAINST PARKINSON'S DISEASE MODEL IN MICE VIA STIMULATION OF GLUCAGON-LIKE PEPTIDE-1

Liu *et al*^[9] investigated the neuroprotective effect and potential mechanisms of sodium butyrate (SB) in a mouse model of Parkinson's disease (PD). A mouse was intraperitoneally treated with 1-methyl-4-phenyl-1, 2, 3, 4-tetrahydropyridine (MPTP) 30mg/kg for 7 consecutive days to induce PD model and SB (200mg/kg) was intragastrically treated for 3 weeks. Dopaminergic degeneration was evaluated by western blot and immunohistochemistry of tyrosine hydroxylase (TH) in the substantia nigra. Brain damage was assessed by histological, apoptosis-associated protein and tight junction proteins studies. The results showed that SB improved neurobehavioral impairment including cognitive behavior and coordination performance. Moreover, SB treatment prevented the MPTP-induced dopaminergic degeneration and decreased expression level of TH in the striatum. The findings suggest that SB has potential as a novel therapeutic for treatment of PD, and its mechanism was associated with stimulating colonic glucagon-like peptide-1 secretion.

THE ROLE OF PROBIOTICS FOR BRAIN HEALTH, AND THEIR POTENTIAL AS A PREVENTIVE MEASURE FOR NEURODEGENERATIVE DISEASES SUCH AS PARKINSON'S DISEASE (PD)

Srivastav *et al*^[10] aimed to study the neuroprotective effects of probiotics in two different models of PD. The author evaluated neuroprotective effects of a probiotic cocktail containing *Lactobacillus rhamnosus* GG, *Bifidobacterium animalis* lactis, and *L. acidophilus* in PD models induced by MPTP or rotenone utilizing behavioral tests, immunohistochemistry and neurochemical analysis. Rescuing effects of the probiotics were observed in the setup, which came with increased levels of neurotrophic factors and butyrate in the brain. *L. rhamnosus* GG was identified to be a major contributor to the induction of neurotrophic factors and downregulation of monoamine oxidase B. The author demonstrated that SB attenuated MPTP-induced neuronal loss in the nigrostriatal pathway. Probiotics could ameliorate neurodegeneration at least partially by increasing butyrate level. The data showed the role of probiotics for brain health, and their potential as a preventive measure for neurodegenerative diseases such as PD.

Neuroprotective effect of butyrate in MPTP-induced mice model of PD

Hou *et al*^[11] evaluated the effects of three dominant SCFAs (acetate, propionate and butyrate) on motor damage, dopaminergic neuronal degeneration and underlying neuro-inflammation related mechanisms in MPTP-induced PD mice. Butyrate reached into the midbrain substantia nigra pars compacta and suppressed microglia over-activation. Besides butyrate inhibited the levels of pro-inflammatory factors (IL-6, IL-1 β and TNF α , $p < 0.01$) and iNOS. And butyrate inhibited the activation of NF- κ B and MAPK signaling pathways in the SNpc region. Thus, butyrate could inhibit neuro-inflammation and alleviate neurological damage of PD.

THE ROLE OF GUT-MICROBIOTA-BRAIN AXIS IN THE PATHOGENESIS OF PD

Shan *et al*^[12] examined whether repeated administration of MPTP can influence the neurotoxicity in the striatum and colon, and the composition of gut microbiota and SCFAs in feces of adult mice. There was a negative correlation between the expression of tyrosine hydroxylase (TH) in the striatum and the expression of phosphorylated- α -Syn (p- α -Syn) in the colon, suggesting a role of gut-brain communication. MPTP caused abnormalities in α and β -diversity of gut microbiota in the mice. Furthermore, the relative abundance of the genus *Faecalicatena* in the MPTP-treated group was significantly lower than that of control group. There was a positive correlation between the genus *Faecalicatena* and the expression of TH in the striatum. The data suggest that MPTP-induced increases in colonic p- α -Syn expression might be associated with dopaminergic neurotoxicity in the striatum via gut-microbiota-brain axis.

Gut microbes promote α -synuclein-mediated motor defects and brain pathology

The accumulation and aggregation of amyloid which are a class of protein with unique self-aggregation properties, and their aberrant accumulation can lead to cellular dysfunctions associated with neurodegenerative diseases. Synucleinopathies are one family of amyloid disease, which includes PD, Lewy Body disease and multiple system atrophy. Central to their pathogenesis is the accumulation of the neuronal protein α -Syn into insoluble amyloid aggregation, which ultimately leads to inflammation and neuronal dysfunction. Sampson *et al*^[13] proposed that exposure to microbial amyloids in the gastrointestinal tract can accelerate α -Syn aggregation and disease in the gut and the brain. The author^[14] reported that a gut bacterial amyloid promotes α -Syn aggregation and motor impairment in mice. Synucleinopathies are characterized by aggregation of the protein α -Syn, resulting in motor dysfunction as exemplified by PD. Using mice that overexpress α -Syn, the author reported that gut microbiota are required for motor deficits, microglia activation, and α -Syn pathology. Gut bacteria regulate movement impairments in mice and depletion of gut bacteria reduces microglia activation.

16S RIBOSOMAL RNA GENE SEQUENCING ANALYSIS OF GUT MICROBIOTA IN 223 PATIENTS WITH PD AND 137 CONTROLS ACROSS COUNTRIES

Meta-analysis of gut dysbiosis in PD was carried out by Nishiwaki *et al*^[15] and after adjusting for confounding factors, genera *Akkermanisia* and *Catabacter*, as well as families *Akkermanisiaceae*, were increased, whereas genera *Roseburia*, *Faecalibacterium*, and *Lachnospiraceae* ND3007 group were decreased in PD. The author reported that intestinal mucin layer-degrading *Akkermanisia* is increased and that short chain fatty acid-producing *Roseburia* and *Faeculibacterium* are decreased in PD across countries, such as the United States, Finland, Russia, and Germany.

The lower fecal butyrate and reduced *Roseburia* counts are linked to depressive symptoms in PD patients

Xie *et al*^[16] investigated whether the changes in the gut microbiome and associated metabolites are linked to PD symptoms and epigenetic markers in leucocytes and neurons. The result showed that PD

shares common butyrate-dependent epigenetic changes with certain gastrointestinal and psychiatric disorders, which could be relevant for their epidemiological linkage. In sum, combining metabolite, microbiome, clinical data, and DNA methylation profiling, the author revealed a possible relation between gut microbiome (*Roseburia*, *Romboutsia* and *Prevotella*), metabolite production and epigenetic changes, implicating immune and neural pathways in PD patients with potential impact on depressive symptoms.

ALTERED GUT MICROBIOTA ASSOCIATED WITH THE DEVELOPMENT OF MOTOR COMPLICATION IN PATIENTS WITH ADVANCED PD

In enrolled 223 PD patients with motor complications, Takahashi *et al*^[17] observed some changes in the gut microbiota: *Lachnospiraceae* *Blautia* and *Lactobacillaceae* *Lactobacillus* were significantly decreased and increased, respectively, in the gut microbiota of PD patients. Furthermore, the author group^[18] investigated the random forest models to predict the progression of PD in two years by gut microbiota in 165 PD patients. Decrease of short chain fatty acids-producing genera, *Fusicatembacter*, *Faecilibacterium*, and *Blautia*, as well as an increase of mucin-degrading genus *Akkermansia*, predicted accelerated disease progression. PD patients with marked gut dysbiosis may thus be destined to progress faster than those without gut dysbiosis.

ASSOCIATION OF FECAL AND PLASMA LEVELS OF SCFAS WITH IMPAIRED GUT-BLOOD BARRIER IN PD PATIENTS

Short chain fatty acids (SCFAs) produced by gut microbiota are reduced in feces but paradoxically increased in plasma of patients with PD, which may stem from intestinal wall leakage. Yang *et al*^[19] investigated synchronous changes of SCFAs in feces and plasma of patients with PD, taking constipation as a confounder to better disentangle the SCFA metabolism exclusively associated with PD. The concentrations of fecal and plasma SCFAs in Patients (33 healthy control subjects and 95 patients with PD) were measured using liquid and gas-mass spectrometry, respectively. Gut-blood barrier permeability was assessed by plasma/fecal ratio of SCFAs concentrations and fecal α 1-anitrypsin concentration. Patients with PD displayed decreased concentrations of fecal acetic, propionic and butyric acid and increased concentrations of plasma acetic and propionic acid. Constipation aggravated gut-blood barrier (GBB) permeability in patients with PD. The study showed alterations of fecal and plasma SCFAs in patients with PD that were associated with an impaired GBB and might be aggravated by constipation.

Reduction in fecal SCFAs but increased plasma SCFAs were observed in patients with PD

Chen *et al*^[20] compared fecal and plasma levels of different SCFAs subtypes in patients with PD and healthy controls to delineate their interrelationships and link to gut microbiota changes and clinical severity of PD. Compared with controls, patients with PD had lower fecal but higher plasma concentrations of acetate, propionate, and butyrate. And the abundance of proinflammatory microbes, such as *Clostridiales bacterium* NK3B98 and *Ruminococcus* sp AM07-15, significantly correlated with decreased fecal levels and increased plasma levels of SCFAs, especially propionic acid.

AGGREGATION AMYLOID-B/A-SYNUCLEIN CO-INCUBATION IS A CONSEQUENCE OF THE PROPERTY OF AMYLOID- B TO SERVE AS NUCLEATION INTERFACE FOR A-SYNUCLEIN AGGREGATION

Neurodegenerative diseases are associated with the formation of amyloids in the nervous system. Amyloids of the amyloid- β peptide or the protein α -synuclein are traditionally considered hallmarks of Alzheimer's and Parkinson's diseases, respectively. Vadukul *et al*^[21] provided new evidence about the protein composition of aggregates formed when these two properties are co-present. The author showed that soluble species of amyloid- β can induce the aggregation of α -synuclein. The amyloid fibrils formed under these conditions are solely composed of α -synuclein to which amyloid - β can be found associated, but not as part of the core of the fibrils.

SYNERGISTIC INTERPLAY AMONG ALZ-B, TAU, AND A-SYN IN SEVERAL NEURODEGENERATIVE DISEASES, SUGGESTING PROTEIN TRIUMVIRATE

A-Synuclein (α -Syn) and tau protein (Tau) aggregates are the neuropathological hallmarks of Parkinson's disease (PD) and Alzheimer's disease (AD), respectively, although both pathologies co-occur in patients with these diseases, suggesting possible crosstalk between them. To elucidate the interaction of pathological α -Syn and Tau, Bassil *et al*^[22] investigated increased accumulation of Tau aggregates occur following simultaneous introduction of α -Syn mouse preformed fibrils and AD lysate-derived tau seeds both in vitro and in vivo. The absence of endogenous mouse α -Syn in mice reduces the accumulation and spreading of Tau, while the absence of Tau did not affect the seeding or spreading capacity of α -Syn. These in vivo results are consistent with the in vitro data wherein the presence of Tau has no synergistic effects on α -Syn. The results pointed out to the important role of α -Syn as a modulator of Tau pathology burden and spreading in the brains of AD, Parkinson's disease with dementia, and Dementia with Lewy bodies patients. Sengupta *et al*^[23] reviewed the emerging evidence of A β , tau, and α -Syn aggregation in pathophysiology, and their overlap in a spectrum of neurodegenerative diseases including AD, progressive supranuclear palsy, Pick's disease, corticobasal degeneration, PD, and dementia with Lewy bodies. The author discussed the prognostic advancements made in biomarker and imaging technologies in the triumvirate proteinopathies, and furthermore, the combined therapeutic modality involving biomarkers and imaging techniques for future combinatorial immunotherapeutic targeting more than one protein aggregates.

A LINK BETWEEN INFLAMMATORY BOWEL DISEASES AND PARKINSON'S DISEASE

PD is characterized by α -Synuclein misfolding with subsequent intraneuronal amyloid changes, and selective neurodegeneration. Dumitrescu *et al*^[24] investigated that gut dysbiosis is prevalent in PD and may lead to intestinal inflammation and barrier dysfunction. Calprotectin and zonulin are markers of intestinal inflammation and barrier permeability, respectively. The author evaluated their serum and fecal levels in 22 patients with sporadic PD and 16

unmatched healthy controls. Increased zonulin was found only in the stool samples of 8 PD patients. The finding indicates a link between inflammatory bowel diseases and PD. Brudek^[25] reported that the possible link between IBD and PD is reviewed based on the available literature. Patients with inflammatory bowel disease (IBD) have a higher risk of developing PD compared with non-IBD individuals. Gene association study has found a genetic link between IBD and PD, and an evidence from animal studies suggested that gut inflammation, similar to that observed in IBD, may induce loss of dopaminergic neurons. Based on preclinical models of PD, it is suggested that the enteric microbiome changes early in PD, and gut infections trigger α -synuclein release and aggregation. Aho *et al.*^[26] investigated that intestinal inflammatory responses and reductions in fecal short chain fatty acids (SCFAs) occur in PD, are related to the microbiota and to disease onset, and are not reflected in plasma inflammatory profiles. Some of these relationships are distinct in PD and are sex-dependent. The author revealed potential alterations in microbiota-host interactions and links between earlier PD onset and intestinal inflammatory responses and reduced SCFAs levels, highlighting candidate molecules and pathways which may contribute to PD pathogenesis and clinical presentation.

CASE REPORTS

Case report 1 Remission of the diabetic PD-patient with the drug and aloe vera juice supplement

A 72-years old diabetic female patient who diagnosed PD stage 3 started to take the PD drug and ingest aloe vera juice supplement (AVJ) on Nov. 2017. On Jan. 2018, she remitted diabetes (HbA_{1c}: 6.5; normal < 6.2 and HOMA-R 2.3; normal < 1.6). She remitted diabetes and PD stage 2 on Apr. 2018.

Case report 2 Remission of diabetic PD-patient with stage 3 into PD stage 2

A 79-years old diabetic male patient who diagnosed PD stage 3 took the PD drug and ingested AVJ supplement on Apr. 2016. He remitted diabetes and into PD stage 2 on Apr. 2018.

Case report 3 Remission of PD-patient with stage 3 into PD level 0

A 65-years old female patient who diagnosed PD stage 3 took the PD drug and ingested AVJ supplement on May 2017. She remitted PD stage 0 on July, 2017.

Case report 4 Remission of the drug-induced Parkinsonism

A 56-years old female who worked as a nurse, had depression at age 22 years old and suspended from duty for 2 weeks. At 31-years old she had relapse the depression and was administered tranquilizer, promethazine tablet for 8 years. At 39 years old she had the stillborn baby. She had drug-induced Parkinsonism caused by aripiprazole on July, 2011 and could not move. Since then, she ingested Aloe vera juice (AVJ), but she diagnosed with schizophrenia and stopped ingestion of AVJ. On 2015 she miraculously recovered consciousness-loss with an intravenous drip injection, bladder catheterization and suction after 3 days of the treatment. She continued to ingest AVJ. On March, 2022 she hospitalized 10 days caused by hard work and diagnosed aripiprazole 24mg, depakene 50mg, bipresso 0.25mg, lemborexant 5mg, and ramelteon 8mg. On May, 2022 she tried drug-deprivation in half amount of drug, and applied Kampo medicine: kamishoyosan as sleeping pills, when she could not sleep well. She took AVJ 300-500ml/day and had well 6-7 hour-sleeping. Then she was able to get off the drugs and well-being QOL on July, 2022.

Case report 5 Remission of irritable bowel syndrome with the drug and AVJ ingestion; Drug deprivation

A 57-years old female who had depression and stress from hard work, had repeated abdominal pain; constipation, diarrhea and vomiting. Beside she suffered from deteriorating atopic dermatitis. Her blood examination resulted in ~100/60 in blood pressure, low cholesterol value, HLD; ~70, LDL; ~100, blood glucose; ~80, and normal value of nephric function on May, 2016. She had a severe continued diarrhea and dehydration, and finally diagnosed irritable bowel syndrome (IBS) on end of July, 2016. She became a bedridden person during ~one month in which the drugs in dermatology, gastroenterology, ophthalmology, otolaryngology and gynecology were diagnosed. She could not be well-being and decided to drug complete deprivation on Sep. 2017, and took AVJ 300ml/day. She recovered normal bowel movement and excrement after three days of AVJ ingestion. Then, she continued to ingest AVJ 300ml/day, and had a well-being QOL on July 2022.

DISCUSSION ON CASE REPORTS

Prophylactic effects of the PD drug and AVJ ingestion as an adjuvant were fully expected for mitigation of risk factor in PD patients with diabetes in case report 1, 2 and 3^[27]. In case report 4 prophylactic effect of AVJ ingestion against drug-induced Parkinsonism was expressed and in case report 5 drug deprivation of a polypharmacy patient was discussed. Possible efficacy of the drug and AVJ ingestion as an adjuvant was shown in Parkinson disease patients with diabetes, and a drug-induced Parkinsonism patient, and a IBS patient.

SUMMARY

We reported a novel association between fermented butyrate in Aloe vera gel with α -Synuclein-induced DNA and histone damage in Parkinson's disease patients. In case reports we exhibited the drug efficacy and a possible efficacy of AVJ as an adjuvant through modulating gut microbiota to facilitate the production of butyrate for normal bowel movement and excrement in PD patients with diabetes, drug-induced Parkinsonism patient, and IBS patient.

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