LEMBAR
HASIL PENILAIAN SEJAWAT SEBIDANG ATAU *PEER REVIEW*
KARYA ILMIAH : JURNAL ILMIAH

Judul Karya Ilmiah (Artikel) : Effects of Clear Kefir on Biomolecular Aspects of Glycemic Status of Type 2 Diabetes Mellitus (T2DM) Patients in Bandung, West Java [Study on Human Blood Glucose, c Peptide and Insulin]

Jumlah Penulis : 7 orang

Status Pengusul : J Judiono, Suharyo Hadisaputro, KS Indranila, Bambang Cahyono, Meiny Suzery, Yuliati Widiastuti, Asep Iwan Purnawan

Identitas Jurnal Ilmiah :

a. Nama Jurnal	: Functional Foods in Health and Disease
b. Nomor ISSN	: ISSN: 2160-3855
c. Vol, Nomor, halaman	: Vol. 4 No. 8 p:340-348
d. Edisi	: Agustus 2014
e. Penerbit	: Functional Food science
f. Jumlah halaman	: 8
g. DOI artikel (jika ada)	: -10.31989/ffhd.v4i8.145
h. Alamat web jurnal	: https://www.ffhdj.com/index.php/ffhd/article/view/145
i. Terindeks di	: Web of Science, COPERNICUS
j. Online Turnitin	: https://doc-pak.undip.ac.id/4956/1/Turnitin_Effects_of_Clear_Kefir.pdf

Kategori Publikasi Jurnal Ilmiah (beri ✓pada kategori yang tepat) :
- ☐ **Jurnal Ilmiah Internasional** / Internasional Bereputasi **
- ☐ Jurnal Ilmiah Nasional Terakreditasi
- ☐ Jurnal Ilmiah Nasional/Nasional

Hasil Penilaian *Peer Review* :

Komponen Yang Dinilai	Nilai Maksimal Jurnal Ilmiah			Nilai Akhir Yang Diperoleh
	Internasional / [20]	Nasional Terakreditasi [ ]	Nasional *** [ ]	
a. Kelengkapan unsur isi artikel (10%)	2			2
b. Ruang lingkup dan kedalaman pembahasan (30%)	6			5,5
c. Kecukupan dan kemutahiran data/informasi dan metodologi (30%)	6			5,5
d. Kelengkapan unsur dan kualitas terbitan/ jurnal (30%)	6			6
Total = (100%)	20			19
Nilai Pengusul =			(40% x 19/6)	**1,26**

Catatan penilaian Artikel oleh Reviewer :

a. **Kelengkapan unsur isi artikel** : Unsur isi artikel lengkap Abstrak, Pendahuluan, Metode, Hasil & Diskusi, Referensi. Abstrak ditulis terstruktur dan unsur lain ditulis dengan cukup baik

b. **Ruang lingkup dan kedalaman pembahasan** : Ruang lingkup keilmuan sesuai pengusul. Pembahasan cukup baik dan dibandingkan dengan penelitian2 sebelumnya serta teori dengan referensi yang cukup sesuai.

c. **Kecukupan dan kemutahiran data/informasi dan metodologi:** Penelitian eksperimental dengan desain RCT pre & post test pada pasien dengan DM tipe 2. Data dikumpulkan dengan teknologi yang terstandar baik. Teknik analisis menggunakan uji beda dan dianalisis dengan baik

d. **Kelengkapan unsur dan kualitas terbitan/ jurnal:** Jurnal internasional terindex di WoS

Semarang,

Reviewer 1

Prof. Dr. dr. Tri Nur Kristina, DMM, M.Kes
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Unit kerja : Fakultas Kedokteran Undip
Bidang Ilmu : Ilmu Kedokteran
Jabatan pangkat : Guru Besar

Lamp C.4

LEMBAR
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f. Jumlah halaman	:	8
g.DOI artikel (Jika ada)	:	10.31989/ffhd.v4i8.145
h. Alamat web Jurnal	:	https://www.ffhdj.com/index.php/ffhd/article/view/145/307
i.Terindeks di	:	Web of Science, COPERNICUS
j. Online turnitin	:	https://doc-pak.undip.ac.id/4956/1/Turnitin_Effects_of_Clear_Kefir.pdf

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- [v] Jurnal Ilmiah Internasional
- [ ] Jurnal Ilmiah Nasional Terakreditasi
- [ ] Jurnal Ilmiah Nasional/ Nasional terindeks di DOAJ CABI COPERNICUS** Tidak Terakreditasi

Hasil Penilaian *Peer Review* :

NO	KOMPONEN YG DINILAI	Nilai Maksimal Jurnal Ilmiah: Internasional/internasional bereputasi [20]	Nasional Terakreditasi [ ]	Nasional *** [ ]	Nilai Akhir Yang Diperoleh
a	Kelengkapan unsur isi artikel (10%)	2			 1,8
b	Ruang lingkup dan kedalaman pembahasan (30%)	6			 5,5
c	Kecukupan dan kemutahiran data/informasi dan metodologi (30%)	6			 5,7
d	Kelengkapan unsur dan berkualitas terbitan/ jurnal (30%)	6			 5,5
	Nilai Total = (100%)	20			18,5
	Nilai Pengusul =		40% x ..../6 =		1,23

Catatan Penilaian artikel oleh Reviewer

a. Kelengkapan unsur isi artikel : abstrak lengkap dan informatif. Pendahuluan, metode, hasil, diskusi, kesimpulan tertulis sesuai kaidah ilmiah. Pustaka baru dan relevan, hanya 23 % > 10 tahun

b. Ruang lingkup dan kedalaman pembahasan : ruang lingkup keilmuan sesuai dengan bidang ilmu pengusul. Pembahasan luas dan dalam, dengan dibandingkan penelitian-penelitian terdahulu.

c. Kecukupan dan kemutahiran data/informasi dan metodologi : penelitian randomized pre - post test control group pada pasien DM. Data primer, dari pemeriksaan laboratorium, penilaian dengan Elisa yang terstandar.

d. Kelengkapan unsur dan berkualitas terbitan/ jurnal : Jurnal internasional - web Science, ESCI.

Semarang, 12 September 2020

Reviewer 2

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Bidang ilmu : Ilmu Kedokteran
Jabatan/pangkat: Guru Besar

Functional Foods In Health And Disease

The Functional Foods in Health and Disease (FFHD) is a peer-reviewed, open-access international journal which serves as the journal of the Academic Society for Functional Foods and Bioactive Compounds (ASFFBC). The journal's overall focus is on Functional Food Science, which is a new and unique area of health and nutrition. Although currently a small scientific field, Functional Food Science is quickly expanding as studies show that functional food products can help manage chronic disease and promote overall wellness. This is reflected in our journal's rapidly growing citation score.

The articles we publish include cutting-edge biomedical research and development of functional foods. The goal is to provide research that can lead to the development of functional food products. The actual definition for these functional foods, as provided by the Functional Food Center (FFC) is as follows: "Natural or processed foods that contain biologically-active compounds; which, in defined, effective non-toxic amounts, provide a clinically proven and documented health benefit utilizing specific biomarkers, for the prevention, management, or treatment of chronic disease or its symptoms."

The journal also serves as an excellent resource for: PhD students, professors, public health professionals, medical doctors, dieticians, nutritionists, government representatives (FDA, NIH, USDA) and the general public for information regarding the latest advancements for the prevention, treatment, and management of chronic diseases or its symptoms using functional foods and bioactive compounds including antioxidents, vitamins and many more.

The FFHD journal has been published under the title Functional Foods in Health and Disease since February, 2011. You can submit your manuscripts and cover letter here (/index.php/ffhd/author/submit/1) or directly to the Editorial Office at editor@ffhdj.com as an e-mail attachment. Additional information about submission guidelines can be found here (/index.php/ffhd/about/submissions) and an example cover letter can be found here (https://drive.google.com/file/d/1dDBTVMc0AkuYCbpUM9gsHc3HUZwurLyu/view).

Journal Citation and Indexing

The FFHD journal has been indexed in the **Web of Science** since 2011 and in the Emerging Sources Citation Index (ESCI) since 2015. The ESCI was a new database in the Web of Science that was launched in 2015 by Thomson Reuters. The ESCI aimed to expand the Web of Science publications by including excellent quality, peer-reviewed journals. Around 3,000 journals were selected for the launch, including the FFHD. Since then, a separate organization called Clarivate Analytics has produced the index starting in 2017. In addition, in 2020 the journal was accepted into **Scopus**! All articles from 2011 on have been accepted and indexed within Scopus. The acceptance into both Scopus and Web of Science show strength of the journal and the authors as well as help expand the reach of our published articles.

The FFHD's citation score has more than doubled over the past two years. As of November 2020 our average citations per item is 3.9. This number is calculated by the sum of the times cited count divided by the number of results in the set. Our h-index is 16, which means there are h papers that have each been cited at least h times.

In addition, the FFHD's self-citation percentage is 4.64%. The self-citation percentage reflects the number of times an article published in a journal has cited a previously published article in the same journal.

The FFHD journal is also indexed in Index Copernicus International (ICI). The ICI has indexed over 6,000 journals. Our current value in ICI for 2018 is 88.99. The value is based on a multidimensional parametric assessment, with over 100 assessment criteria.

In addition, we have also been cited in the following databases: Chemical Abstract, EBSCO, and Google Scholar.

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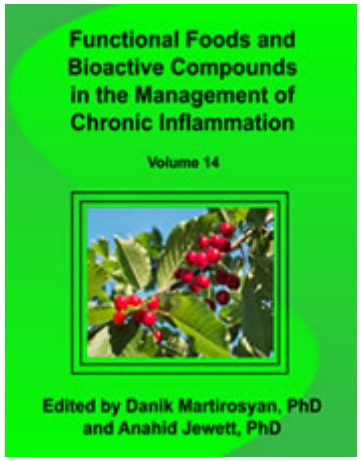

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Research Article Open Access

Evidence-based modeling of mode-of-action for functional ingredients influencing Alzheimer's disease through neurotrophin pathway

Erfan Younesi

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Submission date: May 1, 2014; Acceptance date: August 15, 2014; Publication date: August 23, 2014

ABSTRACT

Background: Brain-derived neurotrophic factor (BDNF) is the most widely expressed member of the neurotrophin family in the human brain and is crucially involved in the development of neural circuits, modulation of synaptic plasticity, and regulation of cognitive functions, including learning and memory. Many studies have shown the association of altered BDNF levels with neurodegenerative and neuropsychiatric disorders. However, BDNF is not able to cross the blood-brain barrier and, thus, its delivery to the nervous system is a challenge. Therefore, functional diets with the ability to induce production of BDNF in the brain may offer an alternative route. The objective of this study was three-fold: first, to find out diets that are causally linked to the agonistic activity of BDNF in the neurotrophin signaling pathway; second and mainly, to investigate mode-of-action of these functional diets through systems-based mechanistic modeling in the context of Alzheimer's disease; and third, to demonstrate the proof-of-concept application of systems biology methods, that are well established in the pharmaceutical sector, to the emerging field of functional food.

Methods: In the first step, two cause-and-effect models of BDNF signaling in two states, i.e. normal state and Alzheimer's disease state, were constructed using published knowledge in scientific literature and pathway databases. A "differential model analysis" between the two states was performed by which mechanistic mode-of-action of BDNF in neurotrophin signaling pathway could be explained with a high molecular resolution in both normal and disease states. The BDNF mode-of-action model was further validated using the "biomarker-guided validation" approach. In the second step, scientific evidence on the effect of various functional diets on BDNF levels and BDNF-related biological processes or outcomes was harvested from biomedical literature using a disease-specific semantic search. This information was then added to the mechanistic model of BDNF mode-of-action and used to substantiate the mode-of-action model.

Results: The differential model analysis resulted in a mechanistic mode-of-action model for

the effector BDNF signaling pathway through NTRK receptors (Neurotrophic tyrosine kinase receptor type 2) in neurons. The model revealed an amyloid-mediated neurotrophin switch mechanism by which the amyloid-beta protein competitively blocks BDNF-NTRK2 downstream signaling under Alzheimer's conditions, thereby "switching" the entire pathway from its normal state with neuroprotective effect to the disease state with a strong push towards neuron apoptosis. This hypothetical switch mechanism was validated by expressed biomarkers as well as empirical data obtained from experimentation of BDNF mimetics in animal models. Several functional diets were found in the literature that showed agonistic effects on the effector BDNF pathway. These effects are exerted through increased levels of BDNF and subsequently, activating the BDNF survival pathway, which leads to similar observations that have been made with BDNF mimetics in animal models.

Conclusions: To our knowledge, this is the first study to investigate mode-of-action of functional foods using systems-based modeling approaches. Moreover, such models can answer the question how functional diets can possibly act at the molecular level and interfere with the disease mechanism. Using scientific evidence supporting such models, there is a possibility to introduce new functional formulations by combining functional ingredients of these diets.

Keywords: evidence-based modeling, mode-of-action, functional ingredient, BDNF, Alzheimer's disease

BACKGROUND

Alzheimer's disease (AD) is a neurodegenerative disorder that leads to cognitive dysfunction due to the loss of neurons in the human brain. This debilitating disease imposes high economic, social and emotional burden, and presently there is no definitive diagnostic or therapeutic solutions for AD.

Neurotrophins and their receptors are among therapeutic candidates that have shown promising results for the treatment of neurological diseases. The neurotrophins are an important family of growth factors that initiate a series of molecular signals on the surface of neurons and induce the survival, development, and function of neurons through "neurotrophin signaling pathway" [1]. BDNF is the most widely expressed member of the neurotrophin family in the human brain, which binds to NTRK2 receptors and activates the neurotrophin signaling. There is accumulated evidence that BDNF exerts broad neuroprotective effects in animal models of Alzheimer's disease [2]. For example, BDNF infusion in rat and mouse has shown to reverse cognitive decline and restore memory [3]. However, neurotrophin proteins cannot be directly applied as therapeutic agents for treatment. They suffer from poor stability in serum, negligible oral bioavailability, and the pleiotropic effects; most importantly, neurotrophins are not able to cross the blood-brain barrier and penetrate the brain [4]. Therefore, to take advantage of therapeutic potential of neurotrophins, there is a need for alternative strategies.

Historically, the concept of "food as medicine" was first suggested by medieval Persian practitioners such as Avicenna and Rhazes who developed scientific guidelines on the use of natural products for treatment of diseases and health problems [5]. Functional diets enriched with natural ingredients are good candidates for circumventing pharmacological problems of

Research Article Open Access

Characterization and specificity of probiotics to prevent *salmonella* infection in mice

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ABSTRACT

Background: Probiotic strains of bacteria can prevent *Salmonella* from causing disease by preventing the pathogen from colonizing the intestines. Two strains of probiotics, *Lactobacillus acidophilius* and *Pediococcus spp*, that were obtained from poultry fecal samples have been shown to be efficacious in poultry. The objective of this study was to determine if these strains of probiotics could prevent salmonellosis in a mouse model.

Methods: First, both strains of probiotics were evaluated for *in vitro* efficacy to inhibit the growth of and interfere with virulence gene regulation in *Salmonella enterica*. For *in vivo* efficacy, mice was used which models Typhoid illness. Mice were divided into 2 groups: Control and treatment, *Lactobacillus* and *Pediococcus* (LP; 10^8 Log CFU). Two experiments were conducted. In the first experiment, the mice were treated with *LP* in water for the first two days of the experiment and challenged with *Salmonella* at day three. In the second experiment, the *LP* treatment was given in the water for 10 days and challenge was performed on day 11. In both experiments, at day 20 post-challenge, all mice were sacrificed, intestinal tracts and organs removed and cultured for *Salmonella*.

Results: The probiotic strains inhibited the growth of *Salmonella* and down-regulation of virulence genes was noted, but dependent on the strain of *Salmonella* being evaluated. For the *in vivo* experiment, the probiotics did not afford the mice protection from infection and increasing the length of time the probiotics were administered did not improve the efficacy of the probiotics.

Conclusions: It appears that these strains of probiotic bacteria are effective against *Salmonella in vitro.* However, these isolates did not afford protection from *Salmonella* infection to mice which may be due to host specifity as these isolates were obtained from poultry.

Keywords: *Salmonella,* Probiotic, *Lactobacillus, Pediococcus,* Mice

BACKGROUND

Bacteria, including *Salmonella,* are becoming resistant to antibiotics making treatment more difficult [1]. Furthermore, antibiotics are retroactive and cannot prevent sequelae including Reiter's syndrome and reactive arthritis. Thus, prevention of infection is key to avoiding life long illnesses. Due to the development of antibiotic resistance, alternatives are being sought which include probiotic bacteria and vaccination. With some consumers, "all natural" prevention methods including probiotics have been more popular [2].

Probiotic bacteria provide a number of benefits to the host including protection from pathogenic bacteria [3]. These bacteria protect the host through several mechanisms including competing for nutrients and niches and production of antimicrobial substances [4,5]. Furthermore, there is evidence that probiotic bacteria can interfere with the gene expression pathways of pathogenic bacteria, which could render the pathogen unable to colonize and cause disease [6].

The performance of probiotic strains may differ with usage in different animals because factors such as adherence sites vary between hosts [2]. It is understood that pathogenic bacteria can be host specific such is the case for many zoonotic bacteria including *Salmonella*. However, it has not been clarified if probiotic bacteria are also host specific. Previous research as well as our own, have demonstrated that a mixed culture of two strains of probiotics are effective at preventing *Salmonella* colonization in broiler chicks [7]. Given the proven efficacy of the probiotic strains used in this study and the source (poultry), the objective of this study was to determine their ability to inhibit *Salmonella* using a Typhoid induced mouse model.

METHODS

Bacteria strains and in vitro characterization

One strain of *Lactobacillus acidophilus* and one strain of *Pediococcus spp.* originally obtained from a poultry cecal sample [7] were the two probiotic bacteria evaluated in this work, were cultured individually in De Man, Rogosa and Sharpe broth (MRS; Thermo Scientific, Pittsburgh, PA) and incubated at 37°C for 24h. After incubation, the medium was passed through a 0.45m filter to produce the sterile spent medium. The pH of the medium was adjusted to 6.2 prior to use. For growth inhibition assays, a total of 11 serovars consisting of 15 strains of *S. enterica* were utilized (Table 1).

All *Salmonella* strains were initially cultured on MRS and incubated at 37°C for 24h. After incubation, a loop of bacteria was inoculated into MRS broth and incubated in a shaking water bath at 37°C for 3h. The cultures then were split into 3 equal aliquots and centrifuged at 8000 × *g* for 5 min. The supernatant was discarded and the pellets were resuspended in sterile MRS or