Floradapt™

Science Based Probiotics for Targeted Health

Kaneka PROBIOTICS

Who is Kaneka

- Kaneka Corp (est. 1949)
- Osaka, Japan
- $5+ Billion in Annual Revenue
- 9,600+ Employees
- Businesses:

  Chemicals, Functional Plastics, Expandable Plastics and Products, Foodstuffs Products, Nutritionals, Life Science Products, Electronic Products, Synthetic Fibers and Others

Kaneka & AB-Biotics Strategic Partnership and Investment

- Kaneka began the investment into AB-Biotics in 2018 and now owns a majority/controlling share (86.6%). AB-Biotics is a Spanish biotech company with 10+ years of research, development and distribution of Probiotic products.
- This culminated a multi year initiative by Kaneka to expand its nutritional business into the growing and developing probiotic market.
- Kaneka's expertise in fermentation, emphasis on clinical research and progress makes it an ideal strategic partner in this space.

KANEKA PROBIOTICS

AB-BIOTICS

Leading the Probiotic Space -Our Global Reach

Populations in developed regions with modern lifestyles lack the necessary microbiome diversity contributing to health.

Uniquely Sourced Strains

- A Proprietary, Patented Strain Collection **of more than 1,000+ different wild-type strains.**
- Origin of Our Strains:
  - Remote Rural Areas
  - Non western-lifestyle – non compromised microbiome.
  - No use of antibiotics or modern hygienic products
  - Sourced from human microbiota

Uniquely Sourced Strains Uncompromised Microbiome

Floradapt Probiotic Formula	Strains Sourced From
Floradapt Gut Comfort	Young healthy children (0-5) in a tropical South American developing region
Floradapt Cardio	healthy infants in a tropical South American developing region
Floradapt Mature Immune Defense	Young healthy children (0-5) mostly fed with vegetables, in a tropical South American developing region
Floradapt Baby Colic, Floradapt Digest	Breast milk and fresh stool samples of healthy people and infants from a tropical South American developing region
Floradapt Gum Health	Saliva children (0-9 yrs.) from a tropical South American developing region

The Kaneka Probiotics Approach

How to Select the Best Strains for Condition X

- Identify pathophysiology of condition X.
- Identify bacterial mechanisms of action (MoA) to target X condition (multiple).
- Select strains receptive to industrial production that excel at the given MoA.
- Verify safety of strains: absence of antibiotic resistances, GRAS status.
- Validate strains by means of randomized, double-blind, placebo controlled clinical trial.

The Advantage of Kaneka

- Science-based strains for a targeted health benefit.
- Formulated with proprietary strains, uniquely selected based on MoA.
- Peer reviewed clinical trials, double blind placebo controlled (gold standard).
- Utilize the actual dosage in the commercial finished product that was administered in the study.
- Shelf stable.
- 24 month stability
- The finished dosage contains the exact formulation, strains and potency used in the clinical trials.

Clinical Strain Formula Advantages

2 billion CFU vs. 20 Billion CFU

- The data and the dose are what matter! Is there clinical data supporting the combination of strains, in a specific modality?
- Are the CFU claims on pack accurate throughout the shelf life?
- Is the CFU level only “at time of manufacturing”?
- Is there published clinical data on the exact probiotic formula supporting health claims?
- Does the formula have verified real time stability?

Probiotic Ingredient Portfolio

L. Plantarum KABP-011 L. Plantarum KABP-012 L. Plantarum KABP-013	Cardio	Cholesterol	
P. Acidilactici KABP-021 L. Plantarum KABP-022 L. Plantarum KABP-023	Gut Comfort	IBS, Gut Anxiety	
P. Pentosaceus KABP-041 B. Longum KABP-042 L. rhamnosus GG (ATCC 53103)	Baby Colic Digest	Colic and Kids Digestive	
L. Brevis KABP-052 L. Plantarum KABP-051 P. Acidilactici KABP-053	Gum Health	Gingivitis & Dental Plaque	
L. Plantarum KABP-031 L. Plantarum KABP-032	Mature Immune Defense	Healthy Aging	
L. Plantarum KABP-062 L. Plantarum KABP-063 L. Plantarum KABP-061	Urinary Tract Vaginal Health	Women's Health	
L.Plantarum DR7 L. Plantarum KABP-023 L. Brevis KABP-052	Brain Mind	Gut-Brain	Under development

11

Probiotics Products Summary

Floradapt Cardio

Cholesterol management and cholesterol reduction

L. plantarum CECT 7527
L. plantarum KABP-011

L. plantarum CECT 7528
L. plantarum KABP-012

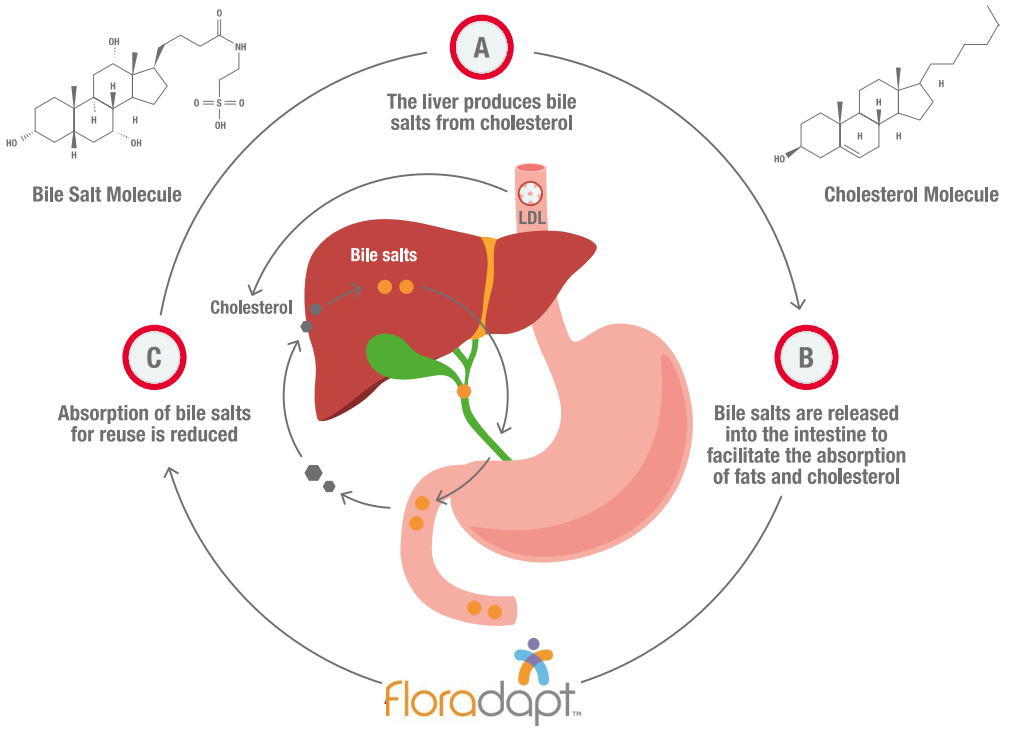
L. plantarum CECT 7529
L. plantarum KABP-013

Multiple Mechanism of Action

Producing the Bile Salt Hydrolase (BSH) enzyme, which degrades bile salts, preventing them from emulsifying cholesterol and thereby hindering its absorption into the blood

Producing Short Chain Fatty Acids (SCFAs), which inhibit the body's own production of cholesterol or remove cholesterol from the blood to the liver

Binding the cholesterol and thereby preventing its absorption into the blood and facilitating its excretion.



Published Clinical Trials

1. Bosch et al (2013) In Vitro Study - A randomized clinical trial evaluating a proprietary mixture of *Lactobacillus plantarum* strains for lowering cholesterol: Conclusion: Combined, these characteristics suggest that these strains could be excellent candidates for reducing high blood cholesterol levels.
2. Fuentes et al. (2016) Clinical Trial in hypercholesterolemia (Med. J. Nutr. Metabol.) Conclusion: The L. plantarum combination reduced LDL-C and improved other lipid parameters, suggesting its potential for hypercholesterolemia treatment.
3. Jumangit et al - An observational, single-center and open-label study to determinate the efficacy and safety of AB-LIFE® alone or adjunct with statins to lower cholesterol levels. : Conclusions: AB-LIFE may contribute significantly to the reduction of serum cholesterol in hypercholesterolemic patients and has a great potential when it is administered alone or combined with other hypocholesterolemic pharmaceuticals such as statins.

Floradapt Cardio Advantages

EFFECTIVE DOSE 1.2 BILLION CFU / DAY (1 CAPSULE)

HIGHEST REDUCTION IN LDL AND TOTAL-C (14-24%)

HIGHER REDUCTION OF TOTAL CHOLESTEROL AGAINST PLACEBO (- ~14%).

INCREASE IN HDL-C.

EFFECT AGAINST DIETARY AND ENDOGENOUS CHOLESTEROL

Supported Health Claims

- Helps maintain cardiovascular function and a healthy circulatory system.
- Supports heart health
- Promotes heart health
- Helps maintain cholesterol levels already in the normal range
- Clinical strains for improving heart health
- Synergistic strains for improving heart health
- A synergistic blend of three strains with three distinct mechanisms documented *in vitro;* these mechanisms are associated with heart health
- Probiotics specifically screened to target heart health
- Patented probiotics
- With a superior triple mechanism documented *in vitro*; these mechanisms are associated with heart health benefits
- Maintains a healthy triglyceride level already in the normal range
- Shown *in vitro* to promote production of short-chain fatty acids (SCFA)
- Promotes healthy gut microflora
- Supports healthy HDL levels already in the normal range
- Supports healthy total cholesterol, LDL and HDL levels already in the normal range
- Supports healthy lipid oxidation status
- Modulates bile metabolism to support healthy cholesterol levels within the normal range (because bile acid affects both dietary lipid absorption and bile production in the body)
- In *in vitro testing,* Floradapt™ proprietary strains outperformed other *Lactobacillus* strains for survival and adhesion to gastrointestinal mucosa
- Outperformed other *Lactobacillus* strains for cholesterol benefits based on a published meta-analysis of 15 selected clinical trials
- Outperformed eight other *Lactobacillus* strains for cholesterol benefits based on a published meta-analysis of 15 selected clinical trials*
- Can be taken only once a day. (Does not need to be taken with every meal.)

Floradapt Gut Comfort

IBS related symptoms, gut inflammation, gut permeability and abdominal discomfort

P. acidilactici CECT 7483

P. acidilactici KABP-021

L. plantarum CECT 7484

L. plantarum KABP-022

L. plantarum CECT 7485

L. plantarum KABP-023

Floradapt™

Floradapt Gut Comfort

Mechanism of Action

What is IBS

- IBS is a functional bowel disorder characterized by recurrent abdominal pain and discomfort associated to altered bowel habits
- Among the top 3 causes of visits to gastroenterologists, affects ~11% of the adult population
- Functional bowel disorders associated with: motility disturbances (spasms and intestinal paralysis), visceral hypersensitivity, altered mucosal and immune function, altered gut microbiota

Mechanism of action

- Production of Short Chain Fatty Acids – Stimulate sodium and water absorption in the colon which reduces diarrhea.
- Production of Acetylcholine (ACh) – Induces anti inflammatory response.
- Production of Polyphosphate (polyP) granules
- Inhibition of opportunistic Gram-negatives (Enterobacteria, Pseudomonas)

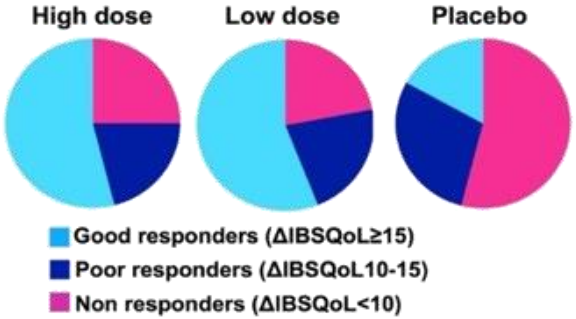
Floradapt™

Floradapt Gut Comfort

Clinical Support

Floradapt Intensive GI improved IBS Quality of Life and Visceral Sensitivity in a randomized, double-blinded trial

N=84



- ✓ The Intensive GI probiotic formula achieves a statistically significant improvement in IBSQoL and VSI vs. placebo in a randomized clinical trial
- ✓ The magnitude of the improvement in IBSQoL is comparable to drugs (Alosetron®, Linaclotide®)
- ✓ Only probiotic to have demonstrated an improvement in Visceral Hypersensitivit, using a validated scale (VSI)

Floradapt™

Competitive Analyses - Probiotics on Quality of Life and Visceral Sensitivity Improvement

PROBIOTIC PRODUCT	IBS CRITERIA	EFFECT ON QoL AND ON VISCERAL SENSITIVITY	STUDY
ALIGN® / ALFLOREX® (*B. infatis* 35624)	Rome II	Effects on IBS-QoL not significant[1] Visceral Sensitivity not assessed	Yuan *et al.* 2017 [17] (meta-analysis)
ACTIVIA® (*B. lactis* DN173001)	Rome II	Only on bowel discomfort domain of FDDQoL[1] Visceral Sensitivity not assessed	Guyonnet *et al* 2007 [19]
L. plantarum 299v®	Rome I Manning Rome III	QoL and Visceral Sensitivity not assessed	Nobaek *et al.* 2000 [20] Niedzielin *et al* 2001 [21] Ducrotte 2012 [22]
GANEDEN BC[30] (*B. coagulans* GBI-30)	Rome II	QoL and Visceral Sensitivity not reported; probiotic and placebo populations significantly differed at baseline	Hun 2009 [23] Dolin 2009 [24]
LACTIBIANE® (*B. longum* LA 101, *L. helveticus* LA102, *L. lactis* LA 103, *S. thermophilus* LA 104)	Rome II	No differences in FDDQoL and SF36 Visceral Sensitivity not assessed	Drouault-Holowacz *et al* 2008 [25]
L. reuteri ATCC55730 (=DSM17938)	Rome II	No differences were found between placebo and probiotic for IBS-QoL	Niv *et al.* 2005 [26]
MUTAFLOR® (*E.coli* Nissle 1917)	Rome II	No effect on QoL; Visceral Sensitivity not assessed	Kruis *et al.* 2012 [27]
BIO-KULT® (14 strains)	Rome III	Effect on QoL at 4 caps/day; Visceral Sensitivity not assessed	Ishaque et al. 2018 [29]
L. reuteri PBS072, *L. acidophilus* PBS066, 0.33 gr inulin	Rome III	22 out of 34 items of the QoL questionnaire (Quality of Life Measure for Persons with IBS) discarded from analysis	Mezzasalma et al. 2016 [32]
AB-BIOTICS I3.1 (*P. acidilactici* CECT7483, *L. plantarum* CECT7484, *L. plantarum* CECT7485)	**Rome III**	**Significant improvement in IBSQoL Significant improvement in Visceral Sensitivity**	**Lorenzo-Zuñiga *et al.* 2014 [12]**

1) Compared to control group. Additional differences may be observed compared to baseline

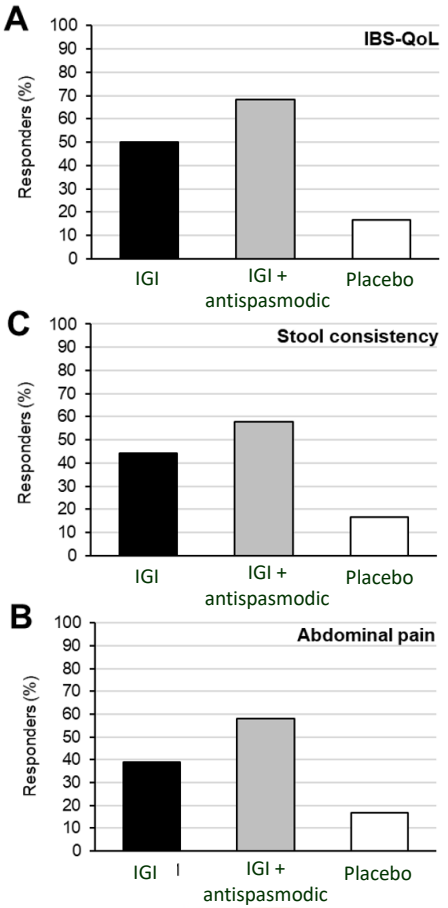
Gut Comfort clinical study 2 (IBS symptom)

Design: Randomized, placebo-controlled trial (3 group parallel)
Subject: People w IBS (Rome IV) (n=55, women, men)
Treatment: Placebo vs IGI, IGI+Antispasmodic for 6 weeks
Evaluation:

- Responder (>50% improvement) rate in
  - IBS-QOL
  - Pain
  - Stool consistency

Result:

- Groups with Probiotics treatments showed better outcome in three evaluation parameters (vs Placebo P<0.01)



Data under journal publish process

Floradapt™

Gut Comfort clinical study 3 (Lactose intolerance)

Design: Randomized, single-blind, Parallel design
Subject: Subject w self-reported lactose intolerance
(n=48, 18-64 y.o., women, men)
Treatment: Placebo vs IGI (3B/d) for 8 weeks
Evaluation:

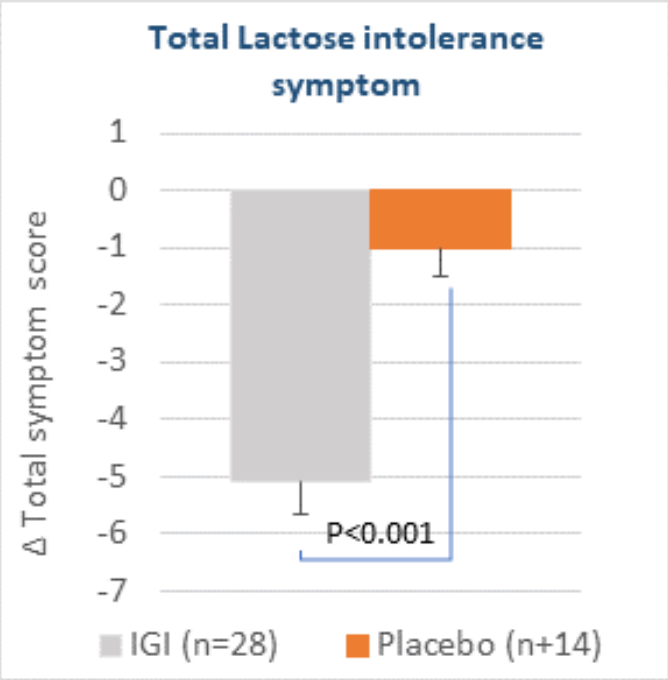
- Primary:
  - lactose intolerance symptom
    (medical questionnaire for Lactose Malabsorption Screening)

- Secondary:
  - LHBT (Lactose hydrogen breath test)
  - Sub-scores for medical questionnaire
    (Diarrhea, Abdominal pain, Vomiting, Intestinal sound, Flatulence)

Data under journal publish process

Clinical outcome – lactose intolerance study

- Improvement of total symptom against placebo.
- Abdominal pain and Flatulence reached significant improvement against placebo
- All secondary end points (except vomiting) showed improvement from baseline only in GC group



Change baseline to wk8	Group	n	Median	Min	Max	P value * (baseline)	P value** (inter group)
Δ diarrhea (score)	IGI	28	0	-4	1	0.006	0.069
	Placebo	14	0	-1	2	0.739	
Δ Abdominal pain (score)	IGI	28	-1	-4	1	<0.001	**0.045**
	Placebo	14	0	-3	1	0.132	
Δ Vomiting (score)	IGI	28	0	-3	1	0.085	0.858
	Placebo	14	0	-1	0	0.157	
Δ Intestinal noises (score)	IGI	28	-1	-4	3	0.002	0.105
	Placebo	14	-0.5	-3	2	0.191	
Δ Flatulence (score)	IGI	28	-2	-4	1	<0.001	**0.004**
	Placebo	14	0	-3	3	1	
Δ AUC (ppm x min: LHBT)	IGI	28	-2250	13380	7890	0.019	0.621
	Placebo	14	-2115	-32700	7020	0.177	

* T-test ** Mann-Whitney test:

Floradapt Gut Comfort

Take-home messages

1) **One capsule a day of Floradapt formula achieves significant reduction of visceral sensitivity and high improvement in QoL (NNT = 2.6).**

2) **First probiotic to demonstrate this effect on visceral sensitivity (underlying problem in IBS) using a specific, validated scale.**

3) **Focus not on pain (drug-like) but on correcting the underlying Visceral Hypersensitivity (gut sensitivity).**

4) **Focus on global QoL improvement because IBS is associated with stress, depression, anxiety and other mood disorders.**

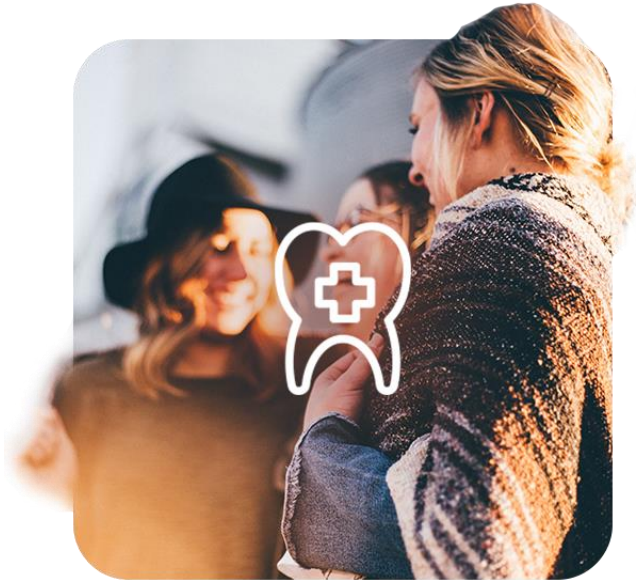
Floradapt Gum Health

Clinical Strains targeting Gum Health

L. plantarum CECT 7481
L. plantarum KABP-051

L. brevis CECT 7480
L. brevis KABP-052

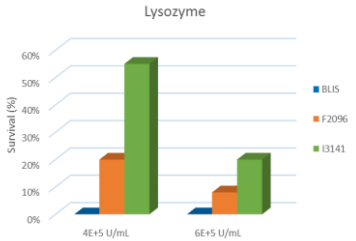
P. acidilactici CECT 8633
P. acidilactici KABP-053



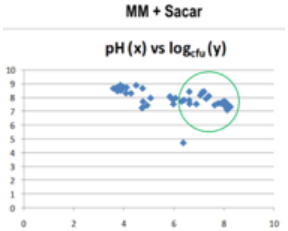
Floradapt™

Floradapt Gum Health

Mechanism of action



Survival to oral conditions and binding to epithelium



Low acidogenic activity

Absence of volatile sulfur compounds

Inhibition of pathogens

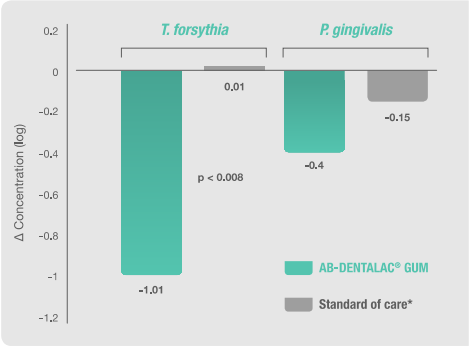
	Antagonism vs. Gingivitis pathogens	Caries prevention	Halitosis prevention	Antiseptic resistance
Lactobacillus plantarum CECT 7481 [a,b]	●	●●●	●●●	●●
Lactobacillus brevis CECT 7480 [a,b]	●	●●●	●●●	●●
Pediococcus acidilactici CECT 8633 [b]	●●●	●●	●●	●●●

a: AB-Dentalac®; b: Dentalac® Gum

** Relevance rating from ● to ●●● for the highest*

Floradapt Gum Health

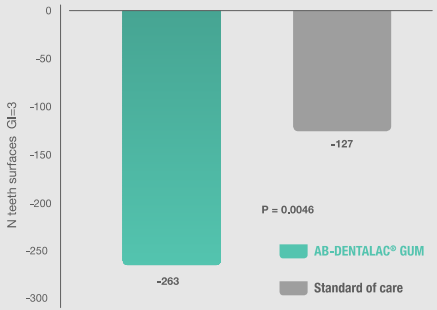
Clinical results



Changes in oral microbiota provide protective effect against gingivitis

Tannerella forsythia displays the strongest association to bleeding and to worsening of gingivitis towards periodontitis.[12]

* professional mechanical plaque removal followed by tooth brushing twice a day with fluorinated toothpaste.



Clinically demonstrated improvement versus the standard of care

Floradapt Gum Health

Main product advantages

Floradapt™

L. plantarum KABP-051
L. brevis KABP-052
P. acidilactici KABP-053

- ✓ Reduces Key pathogens in the mouth; Tannerella forsythia & Porphyromonas gingivalis
- ✓ Clinically tested to be released from gum and achieve colonization
- ✓ Patented probiotic formula specifically targeting dental health
- ✓ Promotes a healthy oral microbiome

BLIS PROBIOTICS™

BLIS K12 ™
Streptococcus salivarius K12

- ❌ No efficacy in reducing pathogens that cause gingivitis
- ❌ Marketing as general oral health due to lack of specific dental health benefits
- ❌ No effect on oral microbiome

Floradapt Gum Health

Take-home messages

1) **Significant reduction in levels of key pathogenic species Tannerella forsythia and Porphyromonas gingivalis in humans.**

2) **Strains clinically tested to be released from gum and achieve colonization.**

3) **Significant reduction of dental plaque in chewing gum with probiotic compared to placebo chewing gum. Correlated with the levels of Lactobacilli.**

Floradapt Baby Colic

Reducing episodes and duration of colic

Clinically Targeting Infant Colic Care

P. pentosaceus CECT 8330

P. pentosaceus KABP-041

B. longum CECT 7894

B. longum KABP-042

Floradapt™

Floradapt Baby Colic

Unique Mechanisms of Action

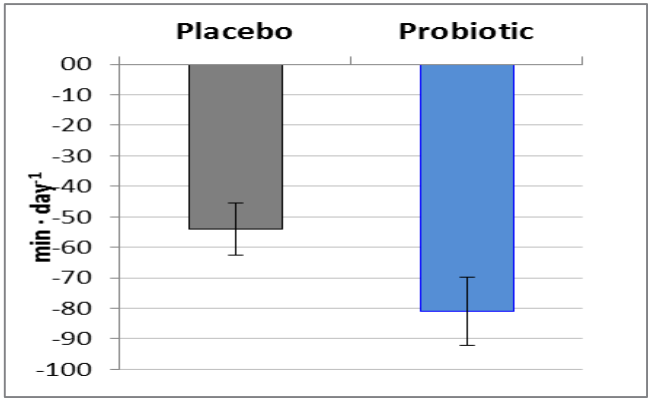
1) **Improves the microflora diversity and prevalence of “good” strains of bacteria by providing “good” bacteria and inhibiting the growth of “bad” bacteria**

2) **Inducing expression of anti-inflammatory molecules**

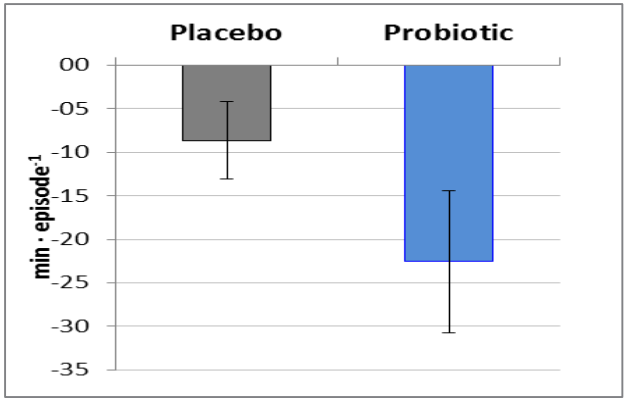
3) **Decreasing the production of gas, both by limiting the growth of “bad” gas-producing bacteria and not contributing gas itself. L.Plantarum.**

Floradapt Baby Colic

Clinical Results



✓ REDUCTION OF DAILY CRYING



✓ REDUCTION OF EPISODE DURATION

- 5 Drops per day
- 67% reduction time in crying in 2 weeks.

Floradapt™

Baby colic clinical study 4 – Recently completed study

3rd study of Baby Colic has recently completed and article is submitted to journal

Design: Randomized, double-blind, placebo-controlled trial
Subject: Breast fed / Formula fed Baby (n=90)
Treatment: Placebo vs Baby colic (1B) for 3 weeks
Evaluation:

- Evaluation is done on the baseline, Day 1st, 7th, 14th 21st
- Primary: Daily duration of crying/fussing
- Secondary: Frequency of Crying/fussing episodes, Fecal consistency/frequency

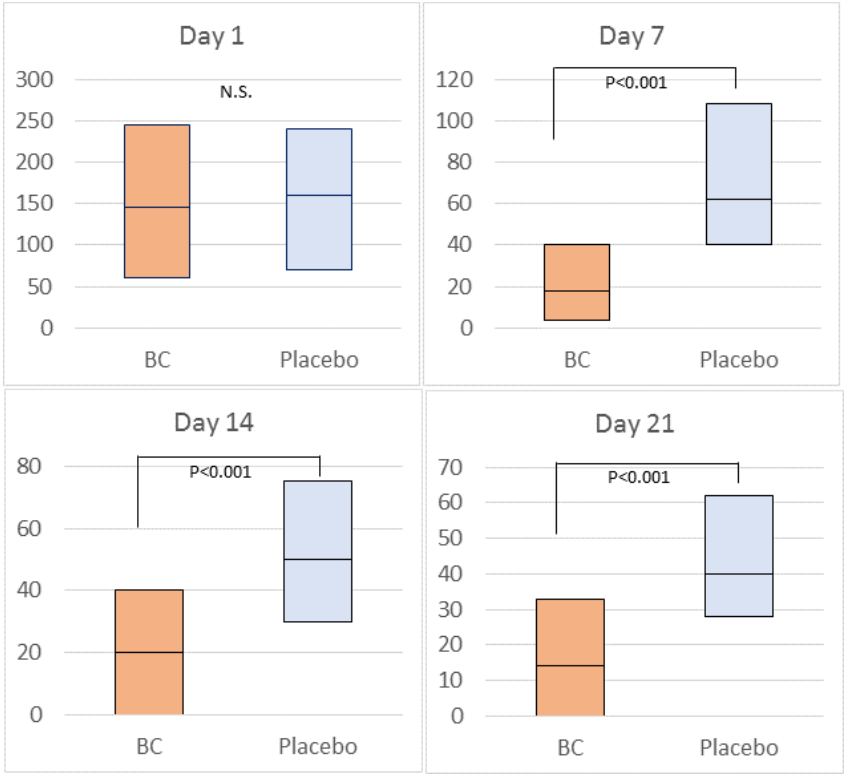
Result:

- Baby colic showed improvement against placebo in :
  - Crying time on 7th, 14th, 21st day (vs. Placebo, P<0.001)
  - Daily crying/fussing frequency on 7th, 14th, 21st day (vs. Placebo, P<0.001)

- Higher responder rate (>50% improve in crying/fussing time) on 7th, 14th, 21st day (vs. Placebo, P<0.01)

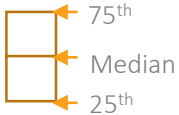
Floradapt™

Representative data



Effect of Floradapt Baby Colic (BC) on crying / fusing time

- Data: Crying time (min./day)
- Data is shown as Median with 25th / 75th percentage



Floradapt Baby Colic

Main product advantages

Floradapt™

P. pentosaceus KABP-041
B. longum KABP-042

- ✓ 5 drops a day of Kolicare® formula achieves significant reduction of crying time (67%)
- ✓ Verified to work regardless of delivery mode and feeding mode (Nursing & Formula)
- ✓ Strains verified for the absence of transmissible antibiotic resistance genes
- ✓ Strains Do not produce gas

BioGaia®

Lactobacillus Reuteri
Protectis (DSM 17938)

- ✗ Strain shown to produce gas in clinical trials
- ✗ No efficacy demonstrated in Formula Fed infants
- ✗ L. reuteri DSM17983 inhibits growth of opportunistic bacteria by producing reuterin

Floradapt Baby Colic

Competitive Product Comparison

	Floradapt™ Baby Colic P. pentosaceus KABP-041 B. longum KABP-042	**Biogaia Reuteri Drops** *L. reuteri* DSM 17938	***Bifidobacterium longum*** **BB-12**	***Lactobacillus rhamnosus*** ***GG ATCC 53103***
			CHR. HANSEN Improving food & health	CHR. HANSEN Improving food & health
Format of Presentation	Removable easy-to-clean dropper	Non-removable dropper	Tablets/caps/formula	Drops/tablets/caps/formula
Strain phenotypic characteristics				
Resistance GI tract	Yes	Yes	Yes	Yes
Immuno-modulatory properties	Very high	High	Very high	High
Antimicrobial activity				
Against pathogens	**High**	**Low**	**High**	**Low**
Against *Bifidobacterium*	**Low**	Not reported	Not reported	Not reported
Strain metabolism	**Homofermentative** **Production of lactic acid** **No gas production**	**Heterofermentative** **Production of gas (CO_2) and lactic acid**	**Heterofermentative** **Production of gas (CO_2) and lactic acid**	**Heterofermentative** **Production of gas (CO_2) and lactic acid**
Efficacy demonstrated for infant colic	**Yes** **Breastfed and formula-fed**	**Yes** **Breastfed only**	**No**	**No**
Baseline crying criteria	>1 hour/day	>3 hour/day	**Not significant**	**Not reported**
Treatment duration	14 days	21-28 days	28 days	**Not reported**

Floradapt™

Floradapt Baby Colic

Take-home messages

1) **67% Reduction in daily crying time.**

2) **Efficacy demonstrated both in nursing and formula fed children, irrespective of delivery mode.**
   Competitive strains have demonsrated efficacy only in nursing children not formula fed. (*L reuteri DSM17938)*

3) **Strains do not produce gas.**
   L reuteri DSM17938 is shown to produce $C0_2$

Floradapt Baby Colic

Proprietary packaging advantages

- Proprietary bottle and dropper design only available through Kaneka.
- Cap is resistant against boiling water. It can be washed / sterilized for hygiene consideration of the infant.
- Our separate cap (one solid cap on vial & attached dropper cap) provides an airtight seal, increasing stability.

Floradapt Digest

Mechanism of action

1) Homofermentative metabolism strains selected for Floradapt Digest do not produce CO2

2) Recovers the positive microbiota (Bifidobacterium and Lactic Acid)

3) Contains L. rhamnosus GG, which enhances GI epithelial structure and function

Floradapt Digest

Symbiotic Probiotic Formula

Floradapt Digest + Lactobacillus GG + Prebiotic FOS + Zinc

Promotes gastrointestinal health by different mechanisms:

1) Helps counter occasional diarrhea

2) Helps restore microbiota diversity

3) Enhances immune system function

Floradapt Digest

Main product advantages

Floradapt™

P. pentosaceus KABP-041
B. longum KABP-042
L. rhamnosus GG

- ✓ Unique Delivery shot delivery system.
- ✓ Designed for treating short episode like diarrhea.
- ✓ Strains Do not produce gas
- ✓ Kaneka L. Rhamnousus GG strain is verified to be genetically identical to the LGG™ source strain.

LGG™ Excellence by Chr. Hansen

Lactobacillus Reuteri Protectis (DSM 17938)

- ✗ standard capsule delivery format
- ✗ L. rhamnoses GG, off patent, generic strain
- ✗ Not designed for short episodes of diarrhea
- ✗ Strain not tested to validate genetic identity

Floradapt Digest

Take-home messages

1) L. rhamnoses GG has level-1 evidence for children's diarrhea and acute adult diarrhea

2) L. rhamnoses GG from AB-Biotics/Kaneka is first strain whose equivalence to the original ATCC53103 strain has been demonstrated

3) Complement L. rhamnoses GG with a B. longum strain to help Bifidobacterium recover after AAD and help ward off opportunistic Enterobacteria

4) Complement L. rhamnoses GG with P. pentosaceus to increase anti-inflammatory activity

Floradapt Digest

Innovative Delivery System

Floradapt™

Floradapt Mature Immune Defense

Immunity boosting for a healthy ageing.

L. plantarum CECT 7315

L. plantarum KABP-031

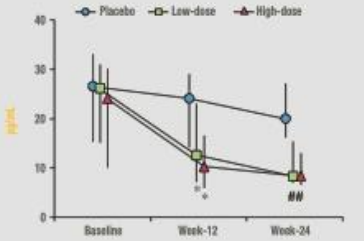
L. plantarum CECT 7316

L. plantarum KABP-032

Floradapt™

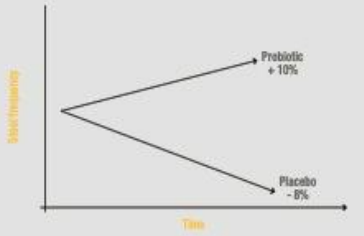
Floradapt Mature Immune Defense

Clinical Results



*Time-course of TGF-β1 concentration in the three groups. *p<0.05 vs. baseline; #p<0.01 vs. baseline. Observed decrease in plasma TGF-β1 concentration associated to AB-Immuno supplementation*

— AB-Immuno formula shows a reduction in the incidence of infections during treatment[4].



The consumption of AB-Immuno formula improves the gastrointestinal transit in the elderly[5].

Improvement of nutritional status: reduces C-Reactive Protein, an inflammation biomarker, and increases protein absorption.

Floradapt Mature Immune Defense

Take-Home Message

1) Clinically shown to boost immune function especially for weaker immune systems through immune cell boosting and flu shot efficiency.

2) Improvement in the digestion and nutrition status in elderly.

3) Addressing major key factors for healthy aging through immune, digestion and nutrition status.

4) L.plantarum KABP-031 and L.plantarum KABP-032 strains showed good adherence properties in the intestine that were twice as good as popular commercial strains L.rhamnosus GG and L.reuteri ATCC 55730.

Floradapt™

Floradapt Brain / Mind

For Anxiety / Stress / Cognition

Floradapt Brain

- **Strain:** L.plantarum DR7
- **MOA:** Modulation of Serotonin synthesis pathway in the body
- **Effective dose**: 1B cfu/day
- **Development status**:
  Science developed (Clinical study published).
  Process development

Floradapt Mind

- **Strain:** L.plantarum KABP-023/ L.brevis KABP-052 (1:1)
- **MOA:** Production of Neuro transmitter by strain (GABA, Dopamine, Acethylcholine)
- **Effective dose**: 1B cfu/day
- **Development status**:
  Process developed (bulk 100B cfu/g available)
  Ongoing two clinical studies

Floradapt™

Strain under development

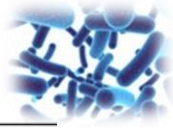
Floradapt™

Condition background

Is there a place for probiotic?

Probiotics in the treatment of depression: science or science fiction?

Timothy G. Dinan, Eamonn M. Quigley



Australian and New Zealand Journal of Psychiatry 2011; 45:1023–1025
DOI: 10.3109/00048674.2011.613766

Prospects & Overviews

It takes guts to grow a brain

Increasing evidence of the important role of the intestinal microflora in neuro- and immune-modulatory functions during development and adulthood

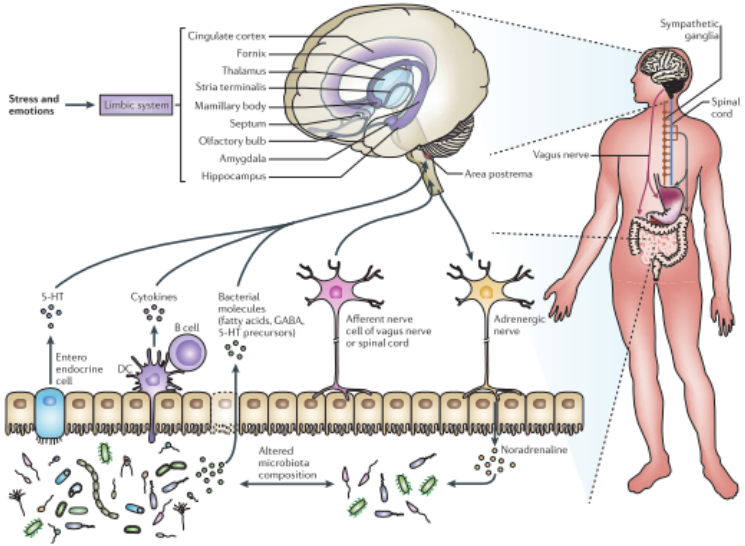
Betty Diamond[1], Patricio T. Huerta[2], Kevin Tracey[3] and Bruce T. Volpe[4]*

Bioessays 33: 588–591,

The interplay between the intestinal microbiota and the brain

nature REVIEWS

Stephen M. Collins, Michael Surette and Premysl Bercik



Potential role of Probiotics on brain/mental health

- Microbiome producing neuro transmitter
- Induction of serotonin (5-HT) production
- Immune modulation

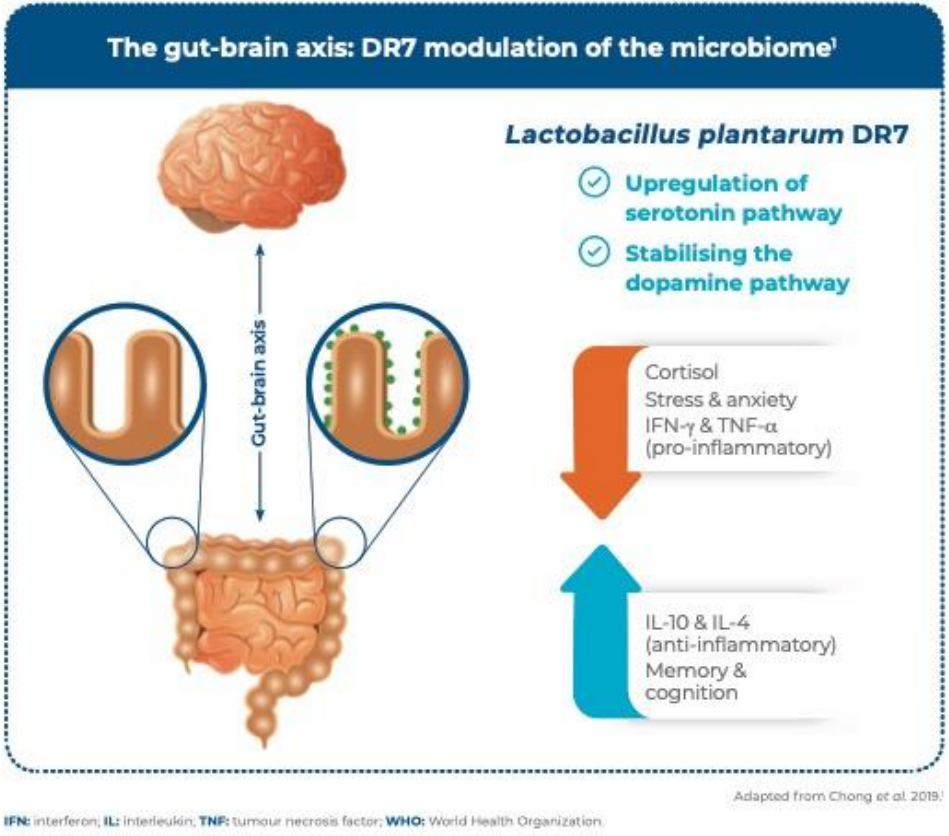
Floradapt™

Floradapt Brain - Mechanism of action

DR7 may exert its effects via mechanisms involving the upregulation of serotonin pathways and by stabilising the pathways of dopamine along the **gut-brain axis**[1]

L.plantrum DR7 can reduce IDO, DBH, TDO and TH, and increase TPH2 and 5-HT6

Modulation of the serotoninergic cascade



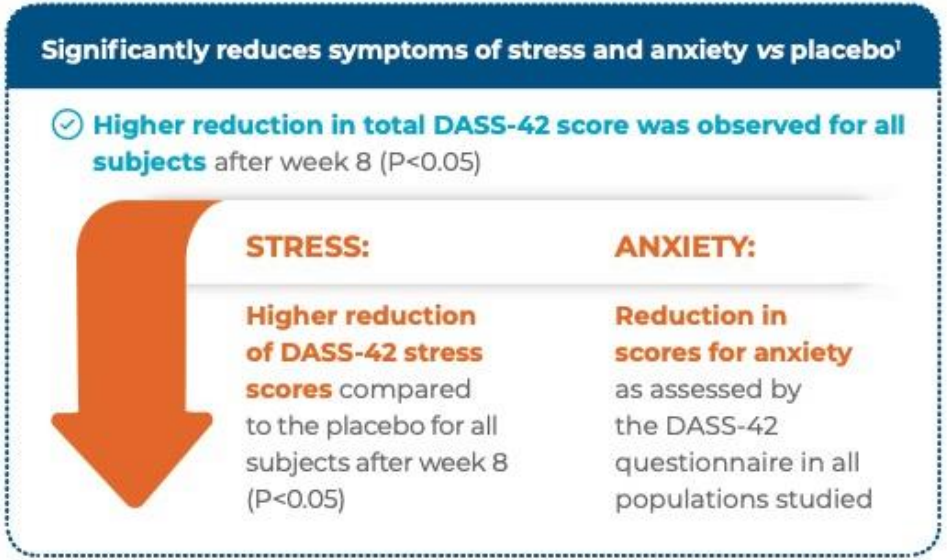
Floradapt™

CLINICAL DATA – Floradapt™ Brain (DR7)

CLINICAL TRIAL RESULTS

(Chong HX et al, Beneficial Microve 2019)

RESULTS OF A DOUBLE-BLIND, RANDOMISED AND PLACEBO-CONTROLLED STUDY N=111 (n=56 DR7 n=55 PLACEBO)[1]



DASS 42 and PSS 10 are two validated questionnaires widely used to determine stress and anxiety levels:

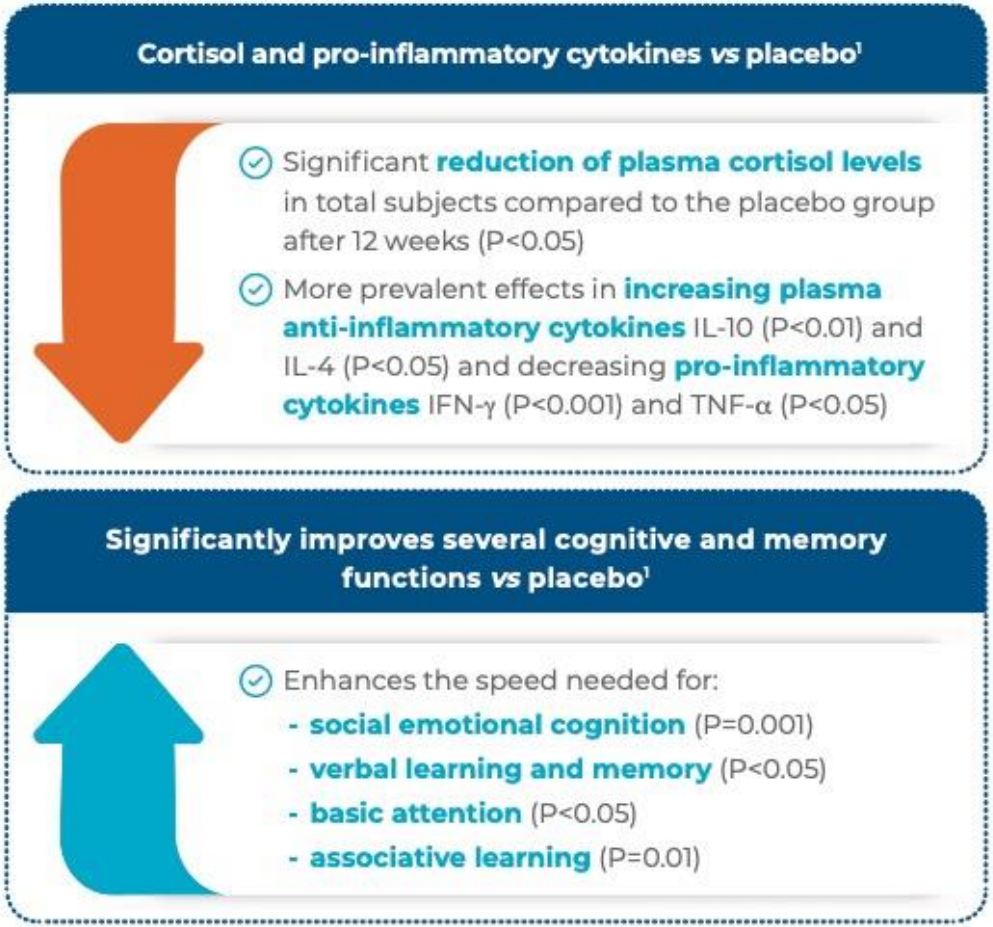
DASS 42[6]

DASS (Depression, Anxiety and Stress Scales) test has **42 self-reporting items** that reflect negative emotional symptoms

PSS 10[7]

PSS (Perceived Stress Scale) test is commonly used to predict both **biological markers** of stress and increased **risk for disease**

Floradapt™



CLINICAL TRIAL RESULTS cont.

- Cognitive function
- Stress / inframmation biomarker marker improvement
- Plasma gene expression analysis confirmed MOA

Floradapt™

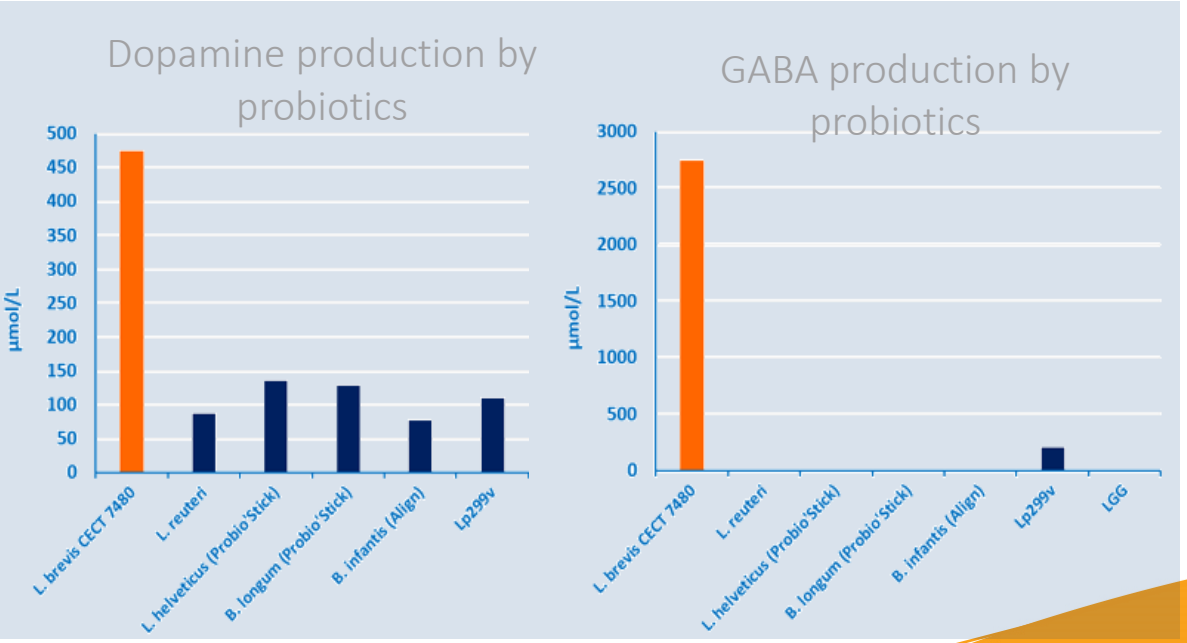
Comparing to competing product

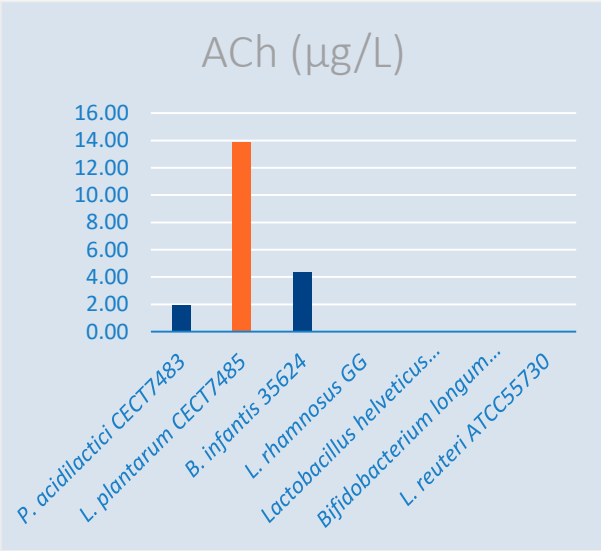
Probiotic	Study	Setup	Clinical Outcome	Biomarker Outcome
L.helveticus R0052 & B.longum R0175	Romijn 2017	RCT study in mild-to-moderate depression with N=79 for 8wk	Totally negative results	Negative
L.helveticus R0052 & B.longum R0175	Messaoudi 2011	RCT study in anxiety with N=55 for 4wk	Improvement in HADS-anxiety and some HSCL-90 subscores	Negative
L.acidophilus R0052 & B.longum R0175	Diop 2008	RCT in stress with N=75 for 3wk	GI symptoms only	Not Assessed
L.plantarum DR7	Min-Tze	RCT in stress with N=111 for 12wk	Improveent in DASS42-anxiety in all ages from wk8 Improvement in DASS42-stress in <30yo from wk8 Improvement in cognition & memory in >30yo	Probiotic changes several relevant biomarkers (cortisol, cytokines and gene expression)

Floradapt™

Floradapt Mind - Mechanism of action

- The strain selection is done based on production of neurotransmitter. P.plantarum KABP-23 (CECT7485) for Ach and L.brevis KABP-52 (CECT7480) for GABA, dopamine
  - KABP-23 also features to produce SCFA relating to anti-inflamation
  - KABP-52 as combination had shown oral pain effect in clinical study





Floradapt™

CLINICAL TRIAL 1 – Recruitment in progress

To investigate the epidemiology of autism spectrum disorders (ASD), social (pragmatic) communication disorders (SPCD) and attention deficit hyperactivity disorder (ADHD) and its relation to nutritional and environmental factors in school population of Tarragona (4-5 yo and 10-11 yo).

- Randomized, placebo-controlled, double-blind clinical trial.
- Subjects will be diagnosed according to DSM-5 criteria by standardized interviews with parents and children.
- Anthropometric and nutritional assessment will be also performed and socio-demographic data and medical history collected

Population: 80 children divided in 2 groups: probiotic group (n=40) and placebo group (n=40).

Treatment: Probiotic/placebo daily administration during 3 months.

Primary Endpoint: Changes in the severity of symptoms.

Floradapt™

CLINICAL TRIAL 2 — Recruitment in progress

To demonstrate Floradapt Mind formula enhances concentration, learning and memorization. This study will include 18-25 year old adults (N=80), during exam period in a Spanish University

- Randomized, placebo-controlled, double-blind clinical trial.
- Anthropometric and nutritional assessment will be also performed and socio-demographic data and medical history collected
- Nutritional assessment will be carried out at baseline and end of the study.
- Antibiotic recent history and use during the study period will be collected.

Population: 80 young adults divided in 2 groups: probiotic group (n=40) and placebo group (n=40).

Treatment: Probiotic/placebo daily administration during 6 weeks.

Endpoints: Changes in perceived stress and anxiety, sleep quality, gastrointestinal function (GSRS questionnaire), gastrointestinal quality of life (GIQLI questionnaire), concentration, learning and memorization. Mean of exam scores of both groups.

Floradapt™

Floradapt Brain / Mind

Take-home messages

1) 2 gut-brain probiotics strains are developing

2) Brain had confirmed clinical effect in anxiety, stress and stress.
   MOA of strain is via serotonin induction (Clinically confirmed)

3) Mind formula targets neurotransmitter production by probiotics
   2 clinical studies are on going

4) Product development with customer from early stage can be offered

Floradapt™

PARTNER WITH KANEKA PROBIOTICS TODAY!

- For more information, clinical data, specifications, samples and pricing…
- Eli Rechanik – National Sales Manager, Probiotics
- C: 732-542-5648
- Eli.Rechanik@Kaneka.com

kaneka
The Dreamology Company
—Make your dreams come true—

Floradapt™