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Probiotics for Chronic Kidney Disease: The "RENADYL" story

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♦ Introduction

Chronic Kidney Disease (CKD) is a growing health problem worldwide. CKD patients have high levels of inflammation, and their blood uremic toxins passively diffuse into the bowel. A novel probiotic supplement formulation was developed, after a decade of R&D, for the removal of several uremic toxins diffused and also generated by the gut microbiome. Thus our product 'RENADYL™' is targeted to help and restore/maintain kidney function in CKD patients.

♦ Objectives

1. Gut dysbiosis and inflammation are related to various diseases including Chronic Kidney Disease[1].
2. Chronic Kidney Disease is accompanied by altered gut microbiome[2,3].
3. Some specific probiotic strains can remove uremic toxins, reduce inflammation and restore the gut microflora balance[4,5].

♦ Methods

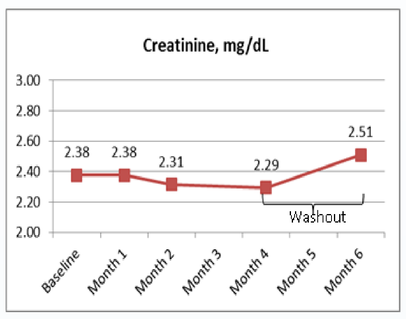
Earlier attempts to genetically engineer a microbe with various genes – urease, creatininase and uricase were technically difficult and unsuccessful. Secondly, the possible challenges from USFDA for use in highly immunocompromised CKD patients led us to drop this route, and opt for naturally occurring safe microbes possessing some uremic toxin catabolizing properties. Screening of 165 probiotics strains, selecting a dozen and enhancing their growth in uremic milieu led to strains which could metabolize uremic toxins. In vitro and simulated gut studies led to the formulation of the probiotic dietary supplement 'RENADYL™' having a blend of three strains of probiotic bacteria; *S thermophilus(KB19)*, *L acidophilus(KB27)* and *B longum(KB31)*. 'RENADYL' has a pharmaceutical like validation with various animal trials[6,7,8] and also human trials in CKD/Dialysis patients.

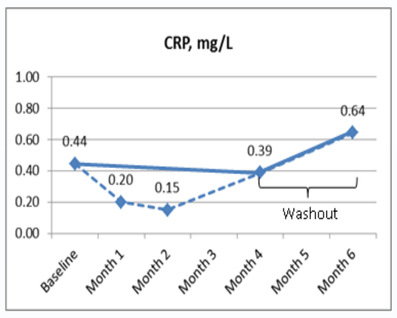
♦ Clinical Trial1-Results

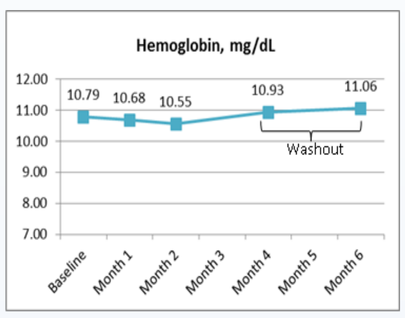
Parameter	No of Patients showing positive response	% of Patients showing positive response	p value
Blood Urea Nitrogen (BUN)	29	63	<0.05
Creatinine (Crn)	20	43	Not statistically significant
Uric Acid	15	33	
Quality of Life	8	86	<0.05

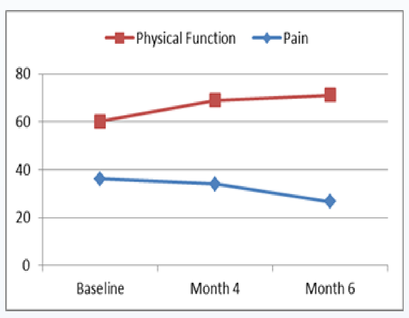
Multi center double blind placebo controlled crossover studies in CKD III and IV patients, for a 6 month period[9].
Dosage of 90 Billion CFU/day.
USA- SUNY and NYU school of Medicine(n=10), Canada-University of Toronto, Scarborough Hospital Ontario (n=13), Nigeria-National Hospital Abuja (n=15), Argentina-Hospital Italiano Bueno Aires(n=8)

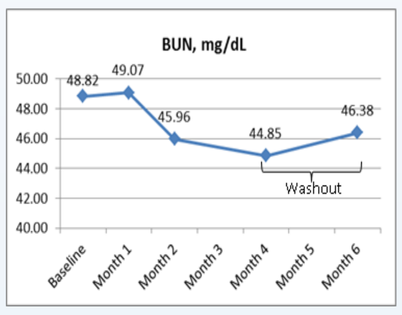
♦ Clinical Trial 2-Results

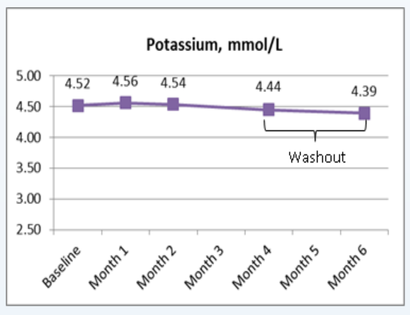












Open label dose escalation study in 28 patients for a period of 6 months at Thomas Jefferson University showed no adverse effects with doses of 90,180 and 270 Billion CFU/day[10]. There was a significant reduction in creatinine and C-reactive protein (CRP) an inflammatory biomarker. Reduction was also seen in urea, potassium and improvement in quality of life (QOL) were also observed.

♦ Clinical Trial 3-Results

Variable	Tx period	N	Mean
White Blood Cells (WBC)	Base	22	6.36
	Placebo (PL)	21	6.07
	Treatment (Tx)	21	5.57
C-reactive protein (CRP)	Base	21	8.89
	Placebo (PL)	18	11.28
	Treatment (Tx)	19	5.1
Total Indoxyl Glucuronide (TIG)	Base	22	0.75
	Placebo (PL)	22	0.75
	Treatment (Tx)	22	0.67

Variable	Tx period	*t* value	Pr>|*t*|
White Blood Cells (WBC)	PL-Tx	2.03	0.0569
C-reactive protein (CRP)	PL-Tx	1.97	0.0707
Total Indoxyl Glucuronide (TIG)	PL-Tx	2.01	0.0579

Double blind placebo controlled crossover studies in 22 dialysis patients over a 6 month period at the State University of New York showed reduction in CRP, serum total Indoxyl glucuronide (IG) and improved QOL with a dose of 180 Billion CFU/day[11].

♦ Summary/Conclusions

Levels of urea, uric acid, creatinine, CRP, and the lesser known toxic metabolite (IG) arising from protein putrefaction due to gut dysbiosis in CKD, can be reduced using some specific probiotic strains with improved QOL. Use of genetically engineered probiotics will be daunting in terms of development costs and US FDA governmental regulations.

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An identical poster was presented at the Harvard probiotic symposium **"Gut Microbiota, Probiotics and Their Impact Throughout the Lifespan"** on September 22-23, 2014 at the Harvard Medical School, Boston, MA.