**INTRODUCTION**

Chronic Kidney Disease (CKD) is a growing health problem worldwide. CKD patients have high levels of inflammation with increased population of pathogenic gut bacteria and, their blood uremic toxins diffuse passively 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 dysbiotics of the gut microbiome to restore CKD function. Our product "RENADYL™" is thus 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.
2. Chronic Kidney Disease is accompanied by altered gut microbiome.
3. Some specific probiotic strains can remove uremic toxins, reduce inflammation and restore the gut microbiota balance.

**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 catalyzing 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 and also human trials in CKD/Dialysis patients.

**RESULTS**

Open label dose escalation study in 28 patients for a period of 6 months at Thomas Jefferson University.

Dosages of 90, 180 and 270 Billion CFU/day.

There was a significant reduction in creatinine and C-reactive protein (CRP), an inflammatory biomarker. Reduction was also seen in urea and potassium. Improvement in quality of life (QOL) was also observed. No adverse effect was seen even with high doses of 270 billion CFU/day.

**REFERENCES**

1. CKD impairs barrier function and alters microbial flora of the intestine: a major link to inflammation and uremic toxicity. Nosratola D Vaziri, Jakk Wong, Madeleine Pahl et al.

Nephrol Dial Transplant, 2014, 0: 1-10


5. Preventing and the Syntometrics: Do They Have a Role in Reducing Uremic Toxins? A Systematic Review and Meta-Analysis. Megan Rossi, David W Johnson et al.

Volume 2012 (2012), Article ID 673631

6. Probiotic Amelioration of Azotemia in 5/6 nephrectomized Sprague-Dawley rats, Naranathan, Natarajan; Patel, Beena; Ranganathan, Pari; Marzely, Joseph; Dhewar, Rahul, Chordia, Tushar; Dunn, Stephen R.; Friedman, Eli A.

The Scientific World JOURNAL, 2005 (5), 652-660

7. In vitro and in vivo Assessment of Intraintestinal Bacteriotherapy Chronic Kidney Disease. Natarajan Ranganathan; Beena G. Patel; Pari Ranganathan; Joseph Marzely; Rahul Dhewar; Bohdan Pechenyak; Stephen R. Dunn; Willy Verstraete; Karel Decroos; Raj Mehta; Eli A. Friedman; N. Ranganathan, E.A. Friedman, Stephen R. Dunn, and Synbiotics: Do They Have a Role in Reducing Uremic Toxins? A Systematic Review and Meta-Analysis. Megan Rossi, David W Johnson et al.


12. Biomark Res 1, 2015, Article ID 568571

---

**RESULTS**

**CLINICAL TRIAL 1**

**CLINICAL TRIAL 2**

**CLINICAL TRIAL 3**

**SUMMARY/CONCLUSIONS**

Levels of urea, uric acid and creatinine, CRP, and the lesser known toxic metabolite (GIL) 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.

---

**FUNDING AND RELATED INFORMATION**

Partial funding for R&D and clinical trials were obtained from NIDDK-NIH, Bethesda, MD, USA and from USAID administered by ICICI Bank, Mumbai, India under the "Technology Development and Commercialization" assistance program. Identical poster presentations were also made for earlier exposure at the Harvard Medical School, Division of Nutrition, Probiotics symposium (Sep 2014) and at Diabetic Kidney Disease: Drug Discovery and Clinical Development Challenges held by the New York Academy of Sciences Dec 2014.