


Creation of a Natural Health Products Database for Assessing Safety in Patients with CKD or Renal Transplant

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Modern Herbal Medicine

- ▶ The World Health Organization (WHO) estimates 80% of people living in some Asian and African countries presently use herbal medicine
- ▶ Common belief among consumers is that NHPs are safe to use as they are “natural”
- ▶ In the EU, NHPs are regulated under the European Directive on Traditional Herbal Medicinal Products
- ▶ In the US, NHPs are regulated dietary supplements by the FDA

Modern Herbal Medicine



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Natural Health Products

Drugs and Health Products

Natural and Non-prescription Health Products

The Natural Health Products Directorate (NHPD) has changed its name to the Natural and Non-prescription Health Products Directorate (NNHPD) subsequent to its recently expanded mandate to include the oversight of non-prescription and disinfectant drugs in addition to natural health products (NHPs). Please note that we are currently modifying documents to reflect this change.

Thank you for your patience and understanding.

A 2010 [©] Ipsos-Reid survey shows that 73% of Canadians regularly take natural health products (NHPs) like vitamins and minerals, herbal products, and homeopathic medicines.

What's New

Subscribe to NHP RSS Feeds

Defining NHPs

- ▶ Under the Health Canada's [Natural Health Products Regulations](#), which came into effect January 1, 2004, NHPs are defined as:

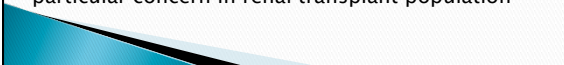
Table 1. Health Canada Criteria for NHP Definition¹

(1) A NHP is defined as any of the following: <ul style="list-style-type: none">(a) Vitamin(b) Mineral(c) Herbal remedy(d) Homeopathic medicine(e) Traditional medicine (e.g. traditional Chinese medicine)(f) Probiotic(g) Other products (e.g. amino acids, essential fatty acids)(h) An extract or isolate with the identical molecular structure of that from the source plant, animal, algae, bacteria or fungi
(2) Additionally, an NHP must be safe to use as an over-the-counter (OTC) product and therefore not require a prescription to be sold

Background

Safety Concerns of NHPs

- ▶ **Unstandardized** nature of many products
- ▶ **Interactions** with prescription medications may result in adverse effects
- ▶ **Altered pharmacokinetics** in patients with chronic kidney disease (CKD)
- ▶ **Nephrotoxicity** in CKD/Tx patients, while dialyzability data for NHPs are quite limited
- ▶ **Immunomodulating effects** of other NHPs are of particular concern in renal transplant population



Objectives

1. To determine:
 - Top NHPs used in the CKD and transplant
 - Demographics of NHP users using the BC Provincial Renal Agency's PROMIS database
 - Compare BC NHP use to published literature
2. To collate literature on safety, drug interactions, immunomodulating activity and PK profiles of NHPs in patients with CKD, dialysis, and renal transplant
3. To create an online database to provide evidence-based recommendations for health-care professionals



Methodology

Objective 1: NHP user demographics and top NHPs used in BC

> Retrospective study using PROMIS database

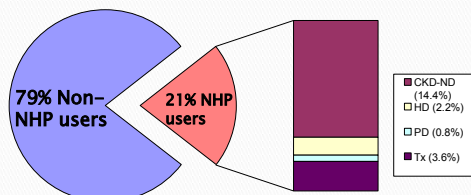
- NHP data entry
- Demographic data of NHP users vs. non-NHP users for non-dialysis CKD (CKD-ND), dialysis and transplant patients
- Literature review on NHP use in renal patients

Demographic Characteristics of BC NHP users

Characteristics	NHP users (n= 4,128)	Non-NHP users (n=15,548)	Statistics
Mean age ± SD (yrs)	69.8 ± 14.5	67.2 ± 17.2	P < 0.001
Male sex (%)	49.0%	56.2%	P < 0.001
Race (%)*			P < 0.001
Caucasian	67.9%	51.6%	
Asian	14.1%	20.6%	
Unknown	9.2%	23.1%	
Health authorities (%)			P < 0.001
IHA	32.6%	67.4%	
NHA	25.3%	74.7%	
FHA	24.7%	75.3%	
VIHA	20.0%	80%	
VCH/PHC	13.4%	86.6%	

*55% of patients registered in PROMIS are caucasian

Proportion of BC NHP users



Demographic Characteristics

Programs	BC	Literature*
CKD-ND	22.3%	25%- 45%
Dialysis	20.0%	2.3%-57%
Tx	17.6%	44-49%

* References at end of presentation

Top NHPs in BC

1. Vitamin B12
2. Omega-3
3. Vitamin C
4. Glucosamine
5. Coenzyme Q10
6. Vitamin E
7. Melatonin
8. Probiotics
9. Cranberry
10. Lutein

Literature Search

Objective 2: Collate literature on NHP use in renal disease and transplant

▶ A literature search and evaluation using:

- *Secondary Sources:*
 - Medline/PubMed Dietary Supplement Subset
 - EMBASE
- *Tertiary Sources:*
 - Natural Medicines
 - Lexi-Natural products
 - Micromedex

Safety Rating System

LIKELY SAFE
Available clinical evidence in a renal disease population showing no significant nephrotoxicity, immunomodulation and/or drug interactions
Also categorized as "Likely Safe" in Natural Medicines

POSSIBLY SAFE
Evidence in a renal population has significant methodological flaws but shows no significant nephrotoxicity, immunomodulation and/or drug interactions
In absence of study in renal population, evidence shows **safety** in general pop'n

POSSIBLY UNSAFE
Evidence in a renal population shows adverse effects, nephrotoxicity, immunomodulation and/or drug interactions
In absence of study in renal population, shows **potential harm** in general pop'n

UNSAFE
Evidence in a renal population shows significant serious adverse effects, nephrotoxicity, immunomodulation and/or DI
In absence of study in renal population, shows **definite harm** in general pop'n

Data Extraction

- 1) Safety (CKD-ND, PD/HD, Transplant)
 - Likely Safe, Possibly Safe, Possibly Unsafe, Unsafe
- 2) Dosing (CKD-ND, Dialysis, Transplant)
- 3) Pharmacokinetics
- 4) Adverse Effects
 - Nephrotoxic effects
 - Other
- 5) Interactions
 - General
 - Immunomodulatory
 - CYP 450
- 6) Literature Summaries - Safety in renal population
 - Clinical Trials (Case Reports, Animal/*In Vitro* studies)
- 7) References

Website



Objective 3: Create an on-line database

- ▶ www.herbalckd.com
 - Fall 2015
 - <http://www.herbalCKD.com>

Limitations – PROMIS data

- ▶ Data relies on NHP data being entered in PROMIS, which may vary between programs
- ▶ Data relies on regular Med Rec routinely integrating questions around use of NHPs
 - ▶ Our study likely under reported NHP usage since studies describe that 50–87.5% of patients do not discuss NHP use with their health care professional^{7,9-10}

Limitations – Website

- ▶ Literature for NHPs in general population is geared toward efficacy data (and not safety)
- ▶ Limited literature exploring efficacy or safety in renal disease and transplant population
- ▶ Some NHPs are combination products, which may confound safety generalizability
- ▶ Non standardized formulations

Conclusions

- ▶ www.herbalckd.com is live on internet
- ▶ HerbalCKD currently contains safety information on most frequently used NHPs
- ▶ HerbalCKD's safety rating system adapted from *Natural Medicines* and clinical trials specific to renal disease or transplant population

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