OP-045 [Apitherapy]

Functional Food Mixture Containing Green Propolis EPP-AF® Extract and Turmeric in Hemodialysis Patients: Preliminary Evidence of Uremic Toxin Modulation and Antioxidant Response

Danielle Nascimento[1,2], Isadora Britto[2], Heloiza Couto[3,4], Livia Alvarenga[2,3], Ludmila F. M. F. Cardozo[3,5], Andresa A. Berretta[6], Marcelo Ribeiro-Alves[x"], Danielle Figueiredo da Cunha[4], Carolina de Oliveira Ramos Petra de Almeida8, Isabela Lemos[3], Mônica Martins Guimarães Guerra[4], Maria E. S. Costa[9], Lia S. Nakao[9], Anderson J. Teodoro[3,8,] Denise Mafra[1,2,3]

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Oxidative stress and gut microbiota–derived uremic toxins are key contributors to complications in patients with chronic kidney disease (CKD), particularly those undergoing hemodialysis (HD). Functional foods with bioactive compounds may represent a complementary strategy to mitigate these processes. This study investigated the effects of a daily mixture of turmeric, green propolis, ginger, and lemon juice on antioxidant status and microbiota-derived uremic toxins in HD patients. A total of 35 patients were enrolled and randomized into two groups: 17 received the functional food intervention (mean age 51 ± 19 years; BMI 23.7 ± 5.4 kg/m²) and 18 received placebo (mean age 51.5 ± 12.2 years; BMI 23.4 ± 3.8 kg/m²). For eight weeks, the intervention group consumed 10 mL of a compound containing Curcuma longa L. (130 mg curcuminoids/day) and standardized green propolis extract (110 mg/day, EPP-AF®), with added ginger and lemon juice, while the placebo group received a matched preparation. Curcuminoids, the main bioactive components of turmeric, present well-documented antioxidant and anti-inflammatory properties but have limited bioavailability due to poor absorption and rapid metabolism. The inclusion of green propolis extract in this mixture was designed to overcome this challenge. Propolis flavonoids enhance the solubility and intestinal absorption of curcuminoids, while turmeric improves the uptake of propolis phenolics, resulting in synergistic bioavailability and efficacy. In addition, preclinical studies demonstrated that this combination exerts immunomodulatory effects: in Nile tilapia, supplementation with turmeric and propolis improved leukocyte activity, upregulated immune-related gene expression, and increased resistance to bacterial infections. These findings reinforce the translational potential of this mixture for populations with impaired immune and redox balance, such as CKD patients. In the present clinical trial, antioxidant capacity was evaluated by oxygen radical absorbance capacity (ORAC), ferric reducing antioxidant power (FRAP), and 2,2-diphenyl-1-picrylhydrazyl (DPPH) assays. Lipid peroxidation was assessed by malondialdehyde (MDA), and high-performance liquid chromatography (HPLC) was used to quantify microbiota-derived uremic toxins. The intervention group showed a significant increase in FRAP values compared with placebo ($p < 0.01$), reflecting improved antioxidant defenses. A trend toward reduced plasma levels of indole-3-acetic acid was also observed. In conclusion, this functional food mixture not only enhanced antioxidant status in HD patients but also addressed the challenge of curcuminoid bioavailability through its synergistic formulation. These preliminary findings warrant larger studies to confirm its role as a supportive strategy in CKD management.

"Functional Food Mixture Containing Green Propolis EPP-AF® Extract and Turmeric in Hemodialysis Patients: Preliminary Evidence of Uremic Toxin Modulation and Antioxidant Response"

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Prescription of Nutritionists
Home prepared

Link para o Vídeo

Background

Lemon

Vitamin C Source

Potent Antioxidant

Immune defense

+

Turmeric

Strong chronic Anti-inflammatory Action

Potent Antioxidant

Metabolic Regulator hepatoprotective

+

Ginger

Digestive
Anti-emetic
Pain Relief

+

Propolis

Broad antimicrobial effect
Anti-inflammatory
Antioxidant
Immune Defense

=

Aims of this Work

- Develop and Characterize a standardized formulation
- Better taste, ready-to-use and stable
- Improve the absorption of the actives
- Demonstration of safety and efficacy – “in vitro”, “in vivo” and clinical

Turmeric Standardized Extract

Turmeric: Limitations

molecular pharmaceutics

reviews

Bioavailability of Curcumin: Problems and Promises

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B. Problems of Curcumin Bioavailability

The reasons for reduced bioavailability of any agent within the body are low intrinsic activity, poor absorption, high rate of metabolism, inactivity of metabolic products and/or rapid elimination and clearance from the body. Studies to date have suggested a strong intrinsic activity and, hence, efficacy of curcumin as a therapeutic agent for various ailments. However, studies over the past three decades related to absorption, distribution, metabolism and excretion of curcumin have revealed poor absorption and rapid metabolism of curcumin that severely curtails its bioavailability. In this section, problems of curcumin bioavailability such as low serum levels, limited tissue distribution, apparent rapid metabolism and short half-life are described in detail.

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NUTRITION JOURNAL

RESEARCH Open Access

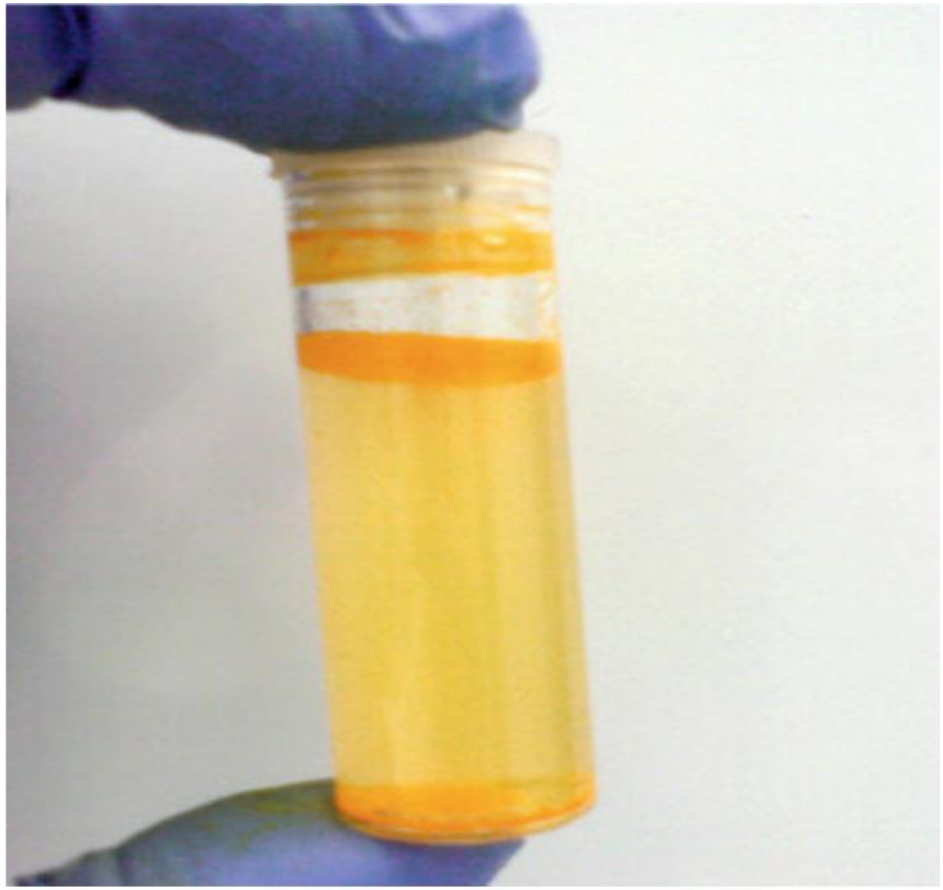
Comparative absorption of curcumin formulations

Ralf Jäger[1*], Ryan P Lowery[2], Allison V Calvanese[2], Jordan M Joy[2], Martin Purpura[1] and Jacob M Wilson[2]

curcumin (ca. 75%), demethoxycurcumin (ca. 15%), and bisdemethoxycurcumin (ca. 5%) [16].

However despite its demonstrated effects, the potential health benefits of curcumin are limited by its poor solubility, low absorption from the gut, rapid metabolism and rapid systemic elimination [17]. While the major portion of ingested curcumin is excreted through the feces unmetabolized, the small portion that is absorbed is extensively converted to its water-soluble metabolites, glucuronides and sulfates. Microbial metabolism of curcumin yields dihydrocurcumin, and tetrahydrocurcumin through NADPH dependent reduction. Curcumin and its reduced metabolites are conjugated with monoglucuronide via beta-glucuronidase, a monosulfate via sulfatase enzymes and a mixed sulfate/glucuronide, resulting

Turmeric: Limitations



Turmeric in powder

Insoluble
Not bioavailable
Not standardized
Low curcuminoids concentration

Green Propolis Standardized Extract (EPP-AF)

Propodry iCaps®

Propolis Standardized EPP-AF – iCaps®

molecules

MDPI

Article

Development and Characterization of High-Absorption Microencapsulated Organic Propolis EPP-AF® Extract (i-CAPs)

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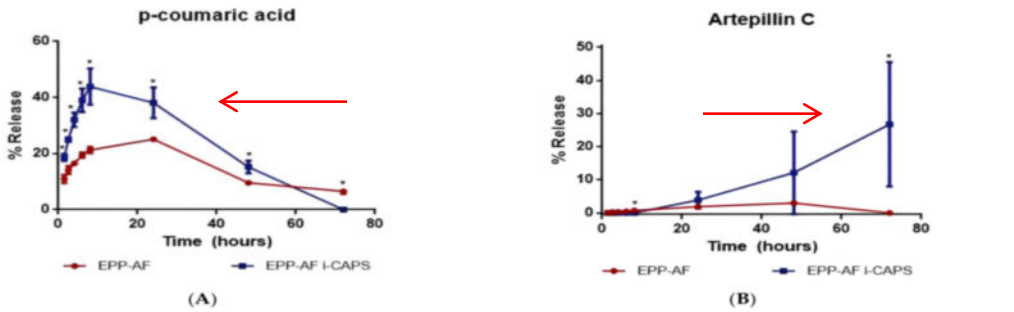

Figure 6. Delivery of the two biomarkers selected for this study, *p*-coumaric acid (**A**) and artepillin C (**B**), from EPP-AF® extract and EPP-AF®-loaded microcapsules ($n = 3$, mean ± standard deviation). * Significantly different ($p < 0.05$).

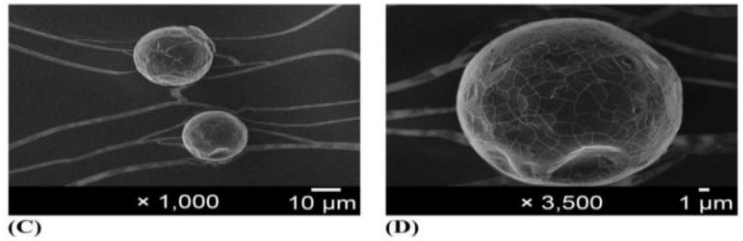

Figure 3. Photomicrographs of organic propolis standardized extract-loaded microcapsules (EPP-AF® i-CAPs) magnified (**A**) 70×, (**B**) 150×, (**C**) 1000×, and (**D**) 3500×.

Technology
Stability
Less Flavor
and Taste

Figure 4. Visual aspect of lyophilized EPP-AF® propolis formulation (**i.A**) and microencapsulated EPP-AF® extract (**i.B**) and of the dispersion of EPP-AF® extract (**ii.A**) and (**ii.B**) EPP-AF® i-CAPS (0.5% *w*/*v* of propolis dry matter) in water.

Solubility

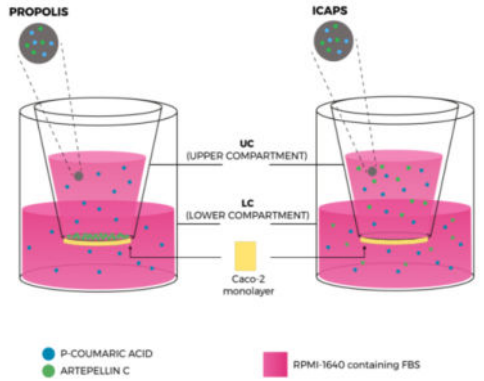

Figure 7. Illustration of the permeable Caco-2 monolayer transport model and results for EPP-AF® (propolis) and EPP-AF® i-CAPS, for the two selected biomarkers, *p*-coumaric acid and artepillin C.

Higher
Absorption

Propolis Standardized EPP-AF – iCaps®

Samples	FRAP (µmol Fe^{II}/mg Propolis Dry Matter) ± SD	DPPH (IC50) (µg Propolis Dry Matter/mL) ± SD
EPP-AF®	2.873 ± 0.045	6.500 ± 0.062
EPP-AF® i-CAPS	2.654 ± 0.062 *	7.342 ± 0.058 *

* Significantly different ($p < 0.05$)—comparison of EPP-AF®-loaded microcapsules with the corresponding EPP-AF® extract.

Table 5. Minimum bactericidal concentration (MBC) obtained with the samples dispersed directly in the Mueller–Hinton agar—results expressed as propolis dry matter (mg/mL) ($n = 3$, mean ± SD).

Samples	MBC (Mean ± SD, mg/mL)					
	S. aureus	*S. aureus* MRSA	*S. epidermidis*	*E. coli*	*K. pneumoniae*	*P. aeruginosa*
EPP-AF® (lyophilized)	55.0 ± 0.0	110.0 ± 0.0	55.0 ± 0.0	110.0 ± 0.0	91.67 ± 31.75	91.67 ± 31.75
EPP-AF® i-CAPS	1.72 ± 0.0 *	5.73 ± 1.98 *	6.88 ± 0.0 *	55.0 ± 0.0 *	27.50 ± 0.0 *	36.67 ± 15.88 *

* Significantly different ($p < 0.05$)—comparison of EPP-AF® i-CAPS and with the corresponding EPP-AF® extract.

Table 6. Determination of cytotoxic and anti-inflammatory activities of EPP-AF® and EPP-AF® i-CAPS ($n = 3$, mean ± SD).

	Cytotoxic Activity (GI_{50}, µg/mL)				Anti-Inflammatory Activity (IC_{50}, µg/mL)
	AGS	Caco-2	MCF-7	PLP2	RAW 264.7
EPP-AF®	184 ± 2 ^{a}	241 ± 20 ^{a}	296 ± 23 ^{a}	146 ± 11 ^{a}	86 ± 3 ^{a}
EPP-AF® i-CAPS	154 ± 1 ^{b}	117 ± 1 ^{b}	271 ± 25 ^{a}	156 ± 4 ^{a}	59 ± 0.1 ^{b}
Elipticin	1.23 ± 0.03 ^{c}	1.21 ± 0.02 ^{c}	1.02 ± 0.02 ^{b}	1.4 ± 0.1 ^{b}	-
Dexamethasone	-	-	-	-	6.3 ± 0.4

GI_{50}—concentration that inhibited 50% of the net cell growth; IC_{50}—sample concentration providing 50% inhibition of Nitric Oxide production. Different letters in each row represent significant differences.

Synergy Studies Propolis and Turmeric to Justify the Composition

Enhanced absorption of prenylated cinnamic acid derivatives from Brazilian green propolis by turmeric in humans and rats

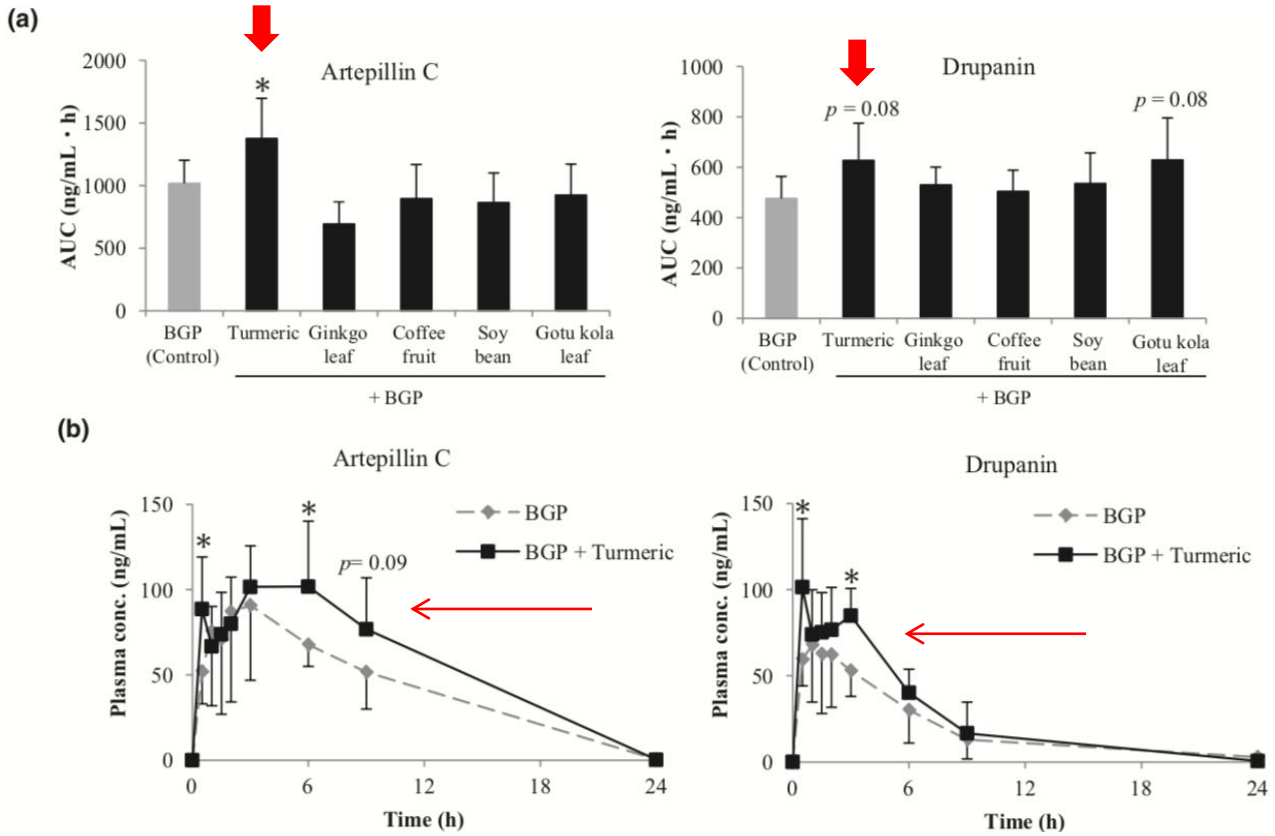

FIGURE 2 (a) Area under the curve (AUC) of the prenylated cinnamic acid derivatives when Brazilian green propolis (BGP) was co-administered with each herbal extract. The AUC was calculated using the trapezoidal rule. (b) Comparison of the plasma concentration–time curve of prenylated cinnamic acid derivatives in the BGP group (control) and the BGP + turmeric group. All data are expressed as mean ± SD, n = eight rats. *$p < .05$ versus BGP (control).

ACS FOOD SCIENCE & TECHNOLOGY

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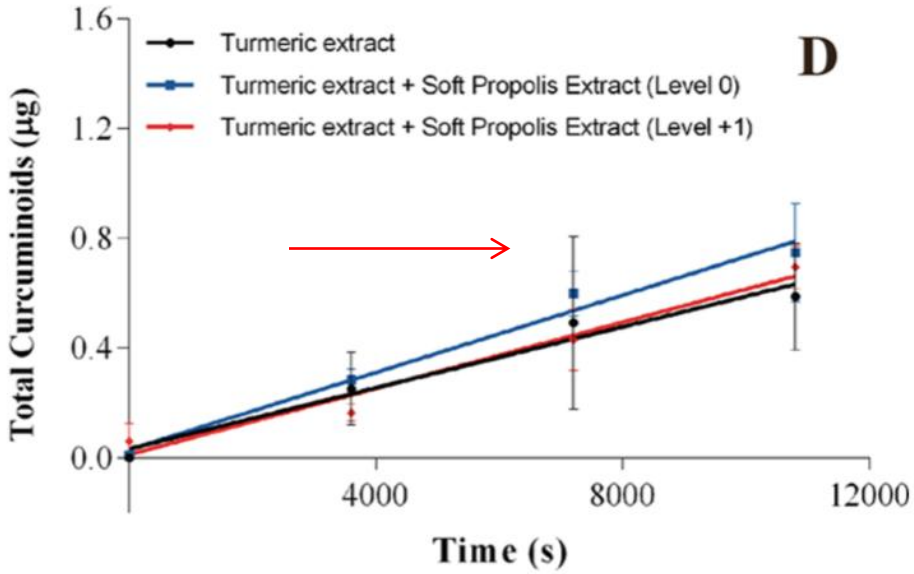
Article

Citrus, Milk Thistle, and Propolis Extracts Improved the Intestinal Permeability of Curcuminoids from Turmeric Extract— an *In Silico* and *In Vitro* Permeability Caco-2 Cells Approach

Nayara Cristina Perez de Albuquerque,○ Maraine Catarina Tadini,○ Ana Luiza Scarano Aguillera Forte, Giulia Ballestero, Thainá Venteu Teixeira, Franciane Marquele de Oliveira,* Mahougnon Siméon Fagnon, Maxime Jouaud, Benjamin Chantemargue, Patrick Trouillas, Andresa Aparecida Berretta,* and Sylvain Kerros*



Development & Characterization

PROPOMAX DAY MORNING SHOT

Aquaculture International (2025) 33:46
https://doi.org/10.1007/s10499-024-01741-8

RESEARCH

Tilápia Model

Dietary intervention of propolis and/or turmeric boosted growth, hematology, biochemical profile, and antioxidant-immune responses and their associated gene expression in Nile tilapia (*Oreochromis niloticus*) challenged with *Edwardsiella tarda*

Mortality Reduction

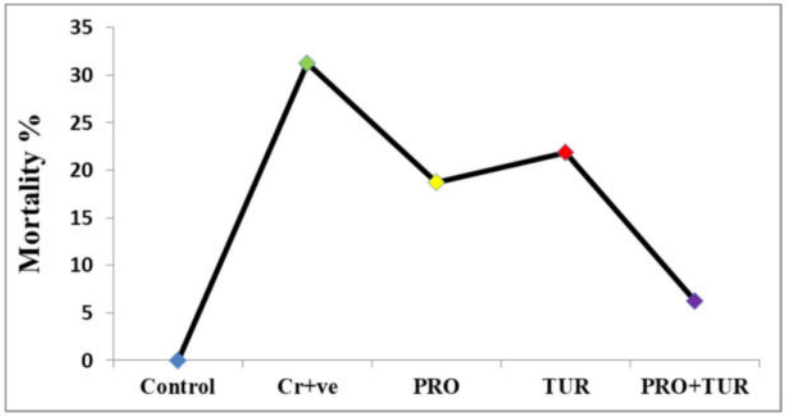


Fig. 1 Mortality % of Nile tilapia during *Edwardsiella tarda* challenge for 7 days. Control, the fish group fed a basal diet and not challenged; Cr+ve, the fish group fed a basal diet and challenged with *E. tarda*; PRO, TUR, and PRO+TUR groups, fish groups fed basal diet contained 1% propolis, 1% turmeric, and a mixture of 1% propolis and 1% turmeric, respectively and challenged with *E. tarda*. Log Rank (Mantel-Cox) = 0.005

Reduction of Inflammatory cytokines

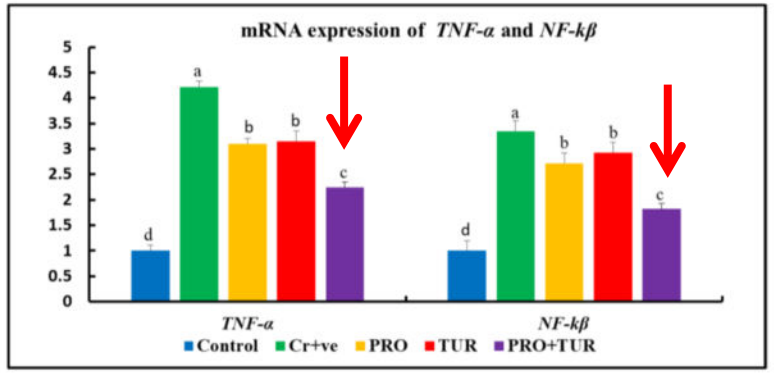


Fig. 2 mRNA expression of the tumor necrosis factor-alpha (*TNF-α*) and nuclear factor kappa B (*NFκB*) of Nile tilapia fed diets supplemented with propolis, turmeric, and their mixture after *E. tarda* challenge. Values in the same bar that did not share the same superscripts are significantly different ($n = 16$/group; $p < 0.05$; one-way ANOVA). Control, the fish group fed a basal diet and not challenged; Cr+ve, the fish group fed a basal diet and challenged with *E. tarda*; PRO, TUR, and PRO+TUR groups, fish groups fed basal diet contained 1% propolis, 1% turmeric, and a mixture of 1% propolis and 1% turmeric, respectively and challenged with *E. tarda*

Increase of Nrf2 and increase immune regulation

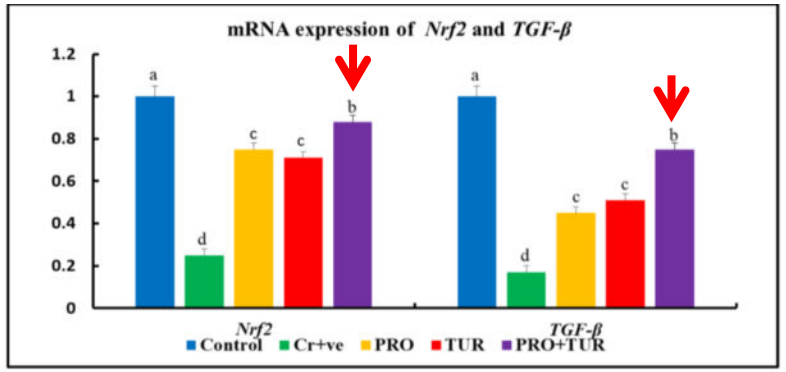


Fig. 3 mRNA expression of the nuclear factor erythroid 2-related factor 2 (*Nrf2*) and transforming growth factor-β (*TGF-β*) of Nile tilapia fed diets supplemented with propolis, turmeric, and their mixture after *E. tarda* challenge. Values in the same bar that did not share the same superscripts are significantly different ($n = 16$/group; $p < 0.05$; one-way ANOVA). Control, the fish group fed a basal diet and not challenged; Cr+ve, the fish group fed a basal diet and challenged with *E. tarda*; PRO, TUR, and PRO+TUR groups, fish groups fed basal diet contained 1% propolis, 1% turmeric, and a mixture of 1% propolis and 1% turmeric, respectively and challenged with *E. tarda*

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RESEARCH ARTICLE

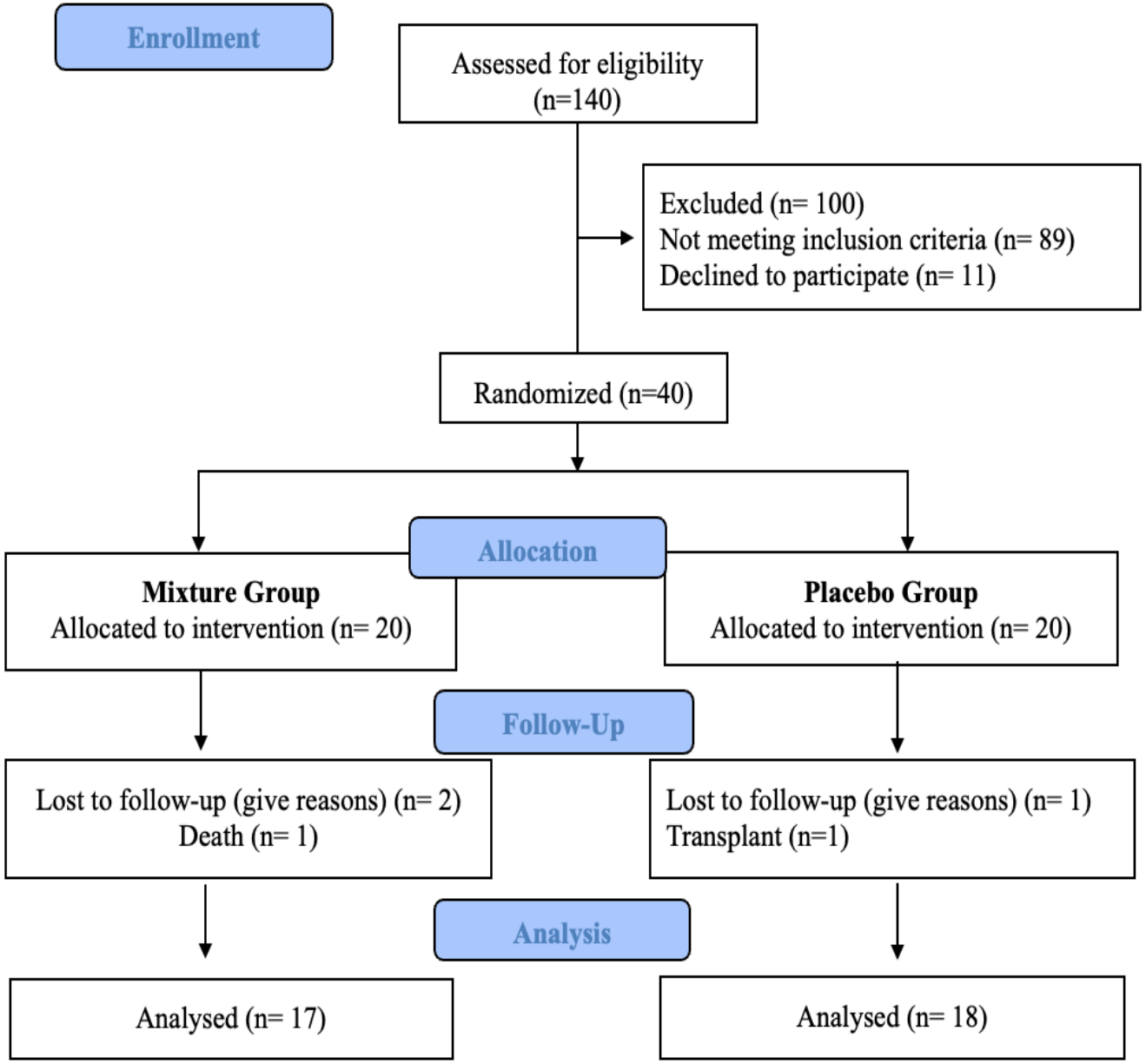
Effects of a Functional Food Mixture on Patients Undergoing Hemodialysis: Preliminary Results Highlighting the Modulation of Uremic Toxins Derived From Microbiota and Antioxidant Markers

Danielle Nascimento[1,2] | Isadora Britto[2] | Heloiza Couto[3,4] | Livia Alv
Andresa A. Berretta[6] | Marcelo Ribeiro-Alves[7] | Danielle Figueiredo da
Almeida[8] | Isabela Lemos[3] | Mônica Martins Guimarães Guerra[4] | M
Anderson J. Teodoro[3,8] | Denise Mafra[1,2,3]

TABLE 1 | Baseline general and anthropometric characteristics of the participants.

Parameters	Overall ($N = 38$)	Placebo ($N = 18$)	Mixture ($N = 20$)	*p* values
Sex (F/M)	17 (44.7%)/21 (55.3%)	9 (50%)/9 (50%)	8 (40%)/12 (60%)	0.770
Age (Years)	51 (17)	51.5 (12.2)	51 (19)	0.951
BMI (kg/m^2)	23.43 (4.5)	23.43 (3.8)	23.7 (5.4)	0.704
HD time (months)	48 (56.7)	57.5 (54)	45.5 (25)	0.217
Kt/V	1.35 (0.33)	1.31 (0.26)	1.41 (0.38)	0.927
Etiology				0.300
Type I diabetes	3 (7.9%)	1 (5.6%)	2 (10%)	
Type II diabetes	4 (10.5%)	3 (16.7%)	1 (5%)	
Hypertension	17 (44.7%)	10 (55.6%)	7 (35%)	
Glomerulonephritis	1 (2.6%)	0 (0%)	1 (5%)	
ADPKD	5 (13.2%)	1 (5.6%)	4 (20%)	
Undetermined	8 (21.1%)	3 (16.7%)	5 (25%)	

Note: Data are presented as median (interquartile range [IQR]) or absolute (relative) proportions.
Abbreviations: ADPKD, autosomal dominant polycystic kidney disease; HD, hemodialysis; Kt/V, dialysis adequacy.



2.3 | Composition of Formulation

One daily dose (10 mL) of the mixture offered was composed of a green propolis standardized extract (EPP-AF) in the microencapsulated presentation [25] in a dose equivalent to 110 mg/day (equivalent to 20 mg of total phenolics as gallic acid), turmeric extract obtained from Active Pharmaceutica with a dosage equivalent to 130 mg curcuminoids/day (equivalent to 100 mg of curcumin), 52 mg of lemon juice in powder, soluble ginger extract (15 mg), xanthan gum, xylitol, and water. The placebo formulation was equivalent to the intervention but did not contain propolis extract and included only 0.1% turmeric extract (equivalent to 7.7 mg of curcumin) as a coloring agent.

TABLE 3 | Dietary intake of patients with CKD undergoing hemodialysis.

Food intake	Overall ($N = 35$)	Placebo ($N = 18$)	Mixture ($N = 17$)	p values
Energy (kcal/day)	1524 (833)	1640.3 (771)	1357.5 (789)	0.264
Energy (kcal/kg/day)	24.8 (14.3)	25.7 (16.6)	22.3 (14.5)	0.389
Proteins (g/day)	67.7 (53.1)	72.4 (52.7)	61.3 (47.0)	0.443
Carbohydrates (g/day)	219.4 (105.2)	232.6 (100.2)	201.8 (101.1)	0.264
Lipids (g/day)	48.7 (24.6)	49.9 (31.8)	47.7 (19.3)	0.593
Monounsaturated (g/day)	13.2 (8.3)	14.4 (10.1)	11.5 (7.1)	0.675
Polyunsaturated (g/day)	8.2 (7.4)	9.0 (6.9)	7.7 (7.7)	0.815
Saturated (g/day)	13.3 (8.98)	12.5 (8.31)	13.6 (9.11)	0.762
Cholesterol (g/day)	161.5 (128.7)	142.2 (132.0)	186 (134.1)	0.393
Calcium (mg/day)	317.0 (295.9)	322.4 (257.4)	312.3 (279.1)	0.331
Iron (mg/day)	10.4 (6.8)	13.0 (8.93)	9.7 (6.9)	0.613
Fiber (g/day)	12.2 (7.7)	12.2 (7.8)	11.9 (7.2)	0.553
Sodium (mg/day)	1635 (969)	1735 (781)	1530 (1017)	0.633
Vitamin A (mcg RAE/day)	244.5 (236.8)	186.3 (324.6)	265.9 (172.3)	0.971
Vitamin C (mg/day)	48.3 (71.8)	44.3 (63.6)	48.3 (76.9)	0.971
Vitamin E (mg/day)	3.2 (2.85)	3.9 (2.7)	2.6 (1.9)	0.427

Note: Data are presented as median (interquartile range [IQR]).

Abbreviations: CKD, chronic kidney disease; RAE, retinol activity equivalents.

TABLE 2 | Biochemical parameters of the groups at baseline.

Biochemical parameters	Overall ($N = 35$)	Placebo ($N = 18$)	Mixture ($N = 17$)	p values
Total cholesterol (mg/dL)	142 (49)	142 (42.5)	151 (52.2)	0.930
High-density lipoprotein (mg/dL)	43 (15.5)	42.5 (10.5)	43 (15.7)	0.510
Low-density lipoprotein (mg/dL)	65.2 (40.5)	78.4 (28.9)	56.4 (51.2)	0.511
Potassium (mg/dL)	5.4 (1.05)	5.4 (1.03)	5.4 (0.9)	0.812
Magnesium (mg/dL)	2.2 (0.4)	2.2 (0.38)	2.2 (0.42)	0.769
Phosphorus (mg/dL)	4.85 (1.78)	4.95 (1.48)	4.65 (1.65)	0.588
Calcium (mg/dL)	9 (0.8)	8.9 (0.58)	9.2 (0.95)	0.305
Triglycerides (mg/dL)	129 (114)	114 (82)	145.5 (128)	0.456
Fasting blood glucose (mg/dL)	94 (50)	93 (30)	96 (61.5)	0.951
Urea (mg/dL)	114 (42.75)	114 (56.5)	115 (38.5)	0.748
Creatinine (mg/dL)	10.27 (3.85)	10.1 (3.0)	10.77 (4.0)	0.762
C-reactive protein (mg/dL)	2.85 (3.22)	2.75 (3.7)	2.85 (2.87)	0.617
Redox status				
MDA (nmol/mL)	1.64 (1.1)	1.48 (1.6)	1.72 (0.8)	0.527
DPPH (mg/dL)	859.14 (47.07)	873.1 (47.34)	850.86 (40.61)	0.430
ORAC (mg/dL)	916.37 (1489.4)	893.3 (1535.0)	916.37 (1431.3)	0.641
FRAP (mg/dL)	10 477 (1638)	10 830 (2475)	10 140 (1365)	0.096
Uremic toxins				
IS (mg/dL)	31.0 (17.5)	29.8 (12.8)	40.4 (29.0)	0.118
pCS (mg/dL)	42.0 (69.4)	31.8 (79.8)	54.8 (46.5)	0.708
IAA (μg/L)	1796.2 (1555.1)	1453.8 (726.2)	2309.5 (2075.5)	0.094

Note: Data are presented as median (interquartile range [IQR]).

Abbreviations: DPPH, 2,2-diphenyl-1-picryl-hydrazyl-hydrate assay; FRAP, ferric reducing antioxidant power; IAA, indole-3-acetic acid; IS, indoxyl sulfate; MDA, malondialdehyde; ORAC, oxygen radical absorption capacity; pCS, *p*-cresyl sulfate.

Antioxidant Activity

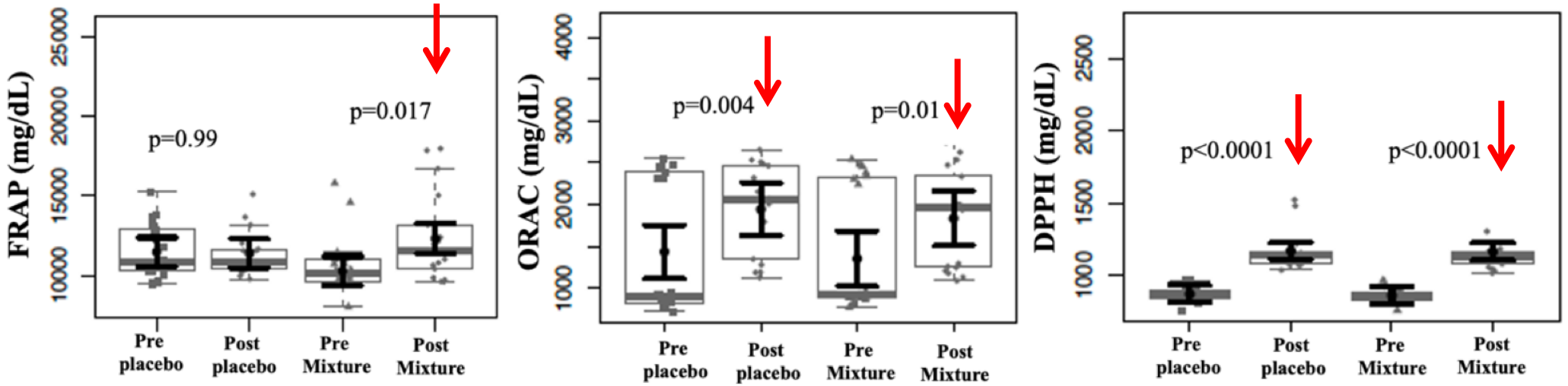
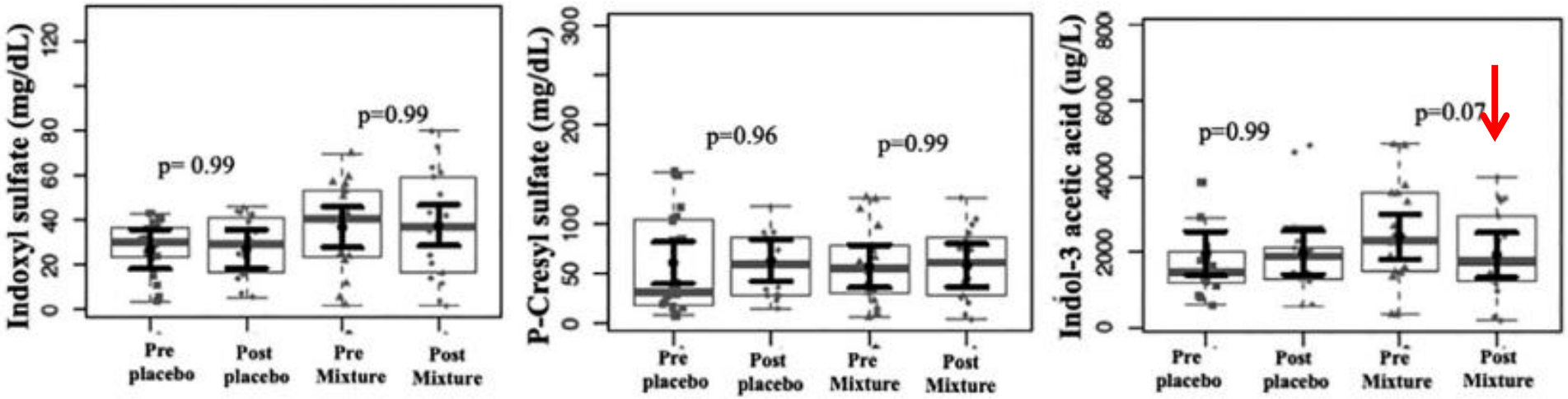


Figure 3: Comparison of the FRAP, ORAC, and DPPH plasma levels in both groups before and after two months of either supplementation with a placebo or a mixture containing turmeric and propolis (intervention).

Uremic Toxins



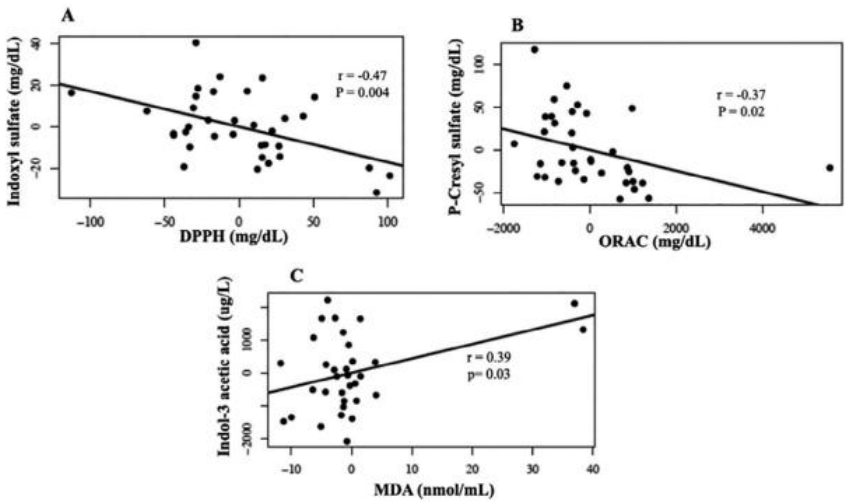


FIGURE 5 | Association between plasma levels of uremic toxins indoxyl sulfate and DPPH (A), *p*-cresyl sulfate and ORAC plasma levels (B), and indole acetic acid and MDA (C) in patients undergoing hemodialysis at the baseline. DPPH, 2,2-diphenyl-1-picrylhydrazyl; MDA, malondialdehyde; ORAC, oxygen radical absorption capacity.

Conclusions

- The formulation was successfully obtained;
- The Synergy between propolis and turmeric was demonstrated with the increase in the absorption of curcuminoids and prenylated compounds;
- Anti-inflammatory, antioxidant and immune defense were demonstrated
- Safety of the Composition and Antioxidant Effects were demonstrated in the clinical trial

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Thank you!

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R&D Leader at Apis Flora Indl. Coml. Ltda, where she has been working for 25 years. **Convenor elected by ISO member countries** to lead the creation of the international standard for propolis and propolis extract. **Board Member** of the International Propolis Research Group (IPRG). **Chair** of the Propolis Group of the International Honey Commission (IHC). **President of ABEMEL** for two terms, currently serving as **Vice-President**.