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Biology-Botany

The consumption of ora-pro-nobis and *tamarillo* improves which health indicators?

O consumo de ora-pro-nóbis e *tamarillo* melhora quais indicadores de saúde?

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ABSTRACT

Ora-pro-nobis and *tamarillo* are unconventional food plants (UFP) in Brazil rich in nutrients and fiber, which can exert positive effects on health. The objective was to analyze studies to verify the effectiveness and applicability of these UFPs in clinical practice. The Prisma protocol was used for data search. Four databases (PubMed, Cochrane, Embase, and Web of Science) were searched using compiled terms and Boolean operators "AND" / "OR." Rayann was used to select the studies. The Joanna Briggs manual was adopted to assess the study's risk of bias. Thus, 17 studies were included in this review. Most studies (14/17) had a low, 2 moderate, and 1 high risk of bias. In conclusion, ora-pro-nobis and *tamarillo* exert beneficial effects on the lipid profile. *Tamarillo* improves antioxidant capacity, besides exerting positive effects on lipid and glycemic profiles, memory, and anticarcinogenic action, while ora-pro-nobis acted in gastrointestinal modulation, lipid profile, body weight reduction, satiety increase, and improving rheumatoid arthritis. To improve health indicators, we suggest daily consumption of 100 g of fresh leaves or 10 g of ora-pro-nobis flour; and/or 100 g of tamarillo.

Keywords: *Pereskia aculeata; Solanum betaceum;* Unconventional food plants; Dietetics; Clinical practice

RESUMO

Ora-pro-nóbis e *tamarillo* são plantas alimentícias não convencionais (PANC) no Brasil ricas em nutrientes e fibras, que podem exercer efeitos positivos à saúde. O objetivo foi analisar estudos para verificar a eficácia e aplicabilidade dessas PANC na prática clínica. O protocolo Prisma foi utilizado para busca de dados. Foram pesquisadas quatro bases de dados (Pubmed, Cochrane, Embase e Web of

Science), utilizando termos compilados, e operadores booleanos “AND”/“OR”. Rayann foi utilizado para selecionar os estudos. O manual de Joanna Briggs foi adotado para avaliar o risco de viés dos estudos. Assim, 17 estudos foram incluídos nesta revisão. A maioria dos estudos (14/17) apresentou baixo risco de viés, 2 moderado e 1 alto. Concluindo, ora-pro-nóbis e *tamarillo* exercem efeitos benéficos no perfil lipídico. *Tamarillo* melhora a capacidade antioxidante, além de exercer efeitos positivos no perfil lipídico, glicêmico, na memória e na ação anticarcinogênica, enquanto a ora-pro-nóbis atuou na modulação gastrointestinal, no perfil lipídico, na redução do peso corporal, no aumento da saciedade e na melhora da artrite reumatoide. Para melhorar os indicadores de saúde, sugerimos o consumo diário de 100 g de folhas frescas ou 10 g de farinha de ora-pro-nóbis; e/ou a partir de 100 g de *tamarillo*.

Palavras-chave: *Pereskia aculeata*; *Solanum betaceum*; Plantas alimentícias não convencionais; Dietética; Prática clínica

1 INTRODUCTION

Interest in the use of alternative sources of underutilized food to improve health, ensure food security and sustainable world development is emerging. These aspects are among the goals to be reached by the United Nations 2030 Agenda (Mariutti et al. 2021). In that respect, unconventional food plants (UFP) are composed of wild edible species that are unknown or rarely consumed by the population (Barbosa et al. 2021). *Pereskia aculeata* Mill. and *Solanum betaceum* Cav. are some types of UFP in Brazil, popularly known respectively as ora-pro-nobis and *tamarillo* or tree tomato. These plants are used in culinary preparations, as potential natural compounds that can help prevent and control chronic non-communicable diseases (Cruz et al. 2021; Maciel et al. 2018; Martin et al. 2021; Orqueda et al. 2017).

Pereskia aculeata contains edible leaves, flowers and fruits. Its leaves are rich in protein, with an amino acid profile similar to that of legumes, besides containing dietary fiber, sterols (sitosterol and stigmasterol), carotenoids, phenolic compounds, vitamins C and B_9, and minerals such as calcium and iron (Garcia et al. 2019; Silveira et al. 2020; Terra & Viera 2019; Vieira et al. 2020). Other UFP *Solanum betaceum* (Syn.: *Cyphomandra betacea* (Cav.) Sendtn., *Cyphomandra crassifolia* (Ortega) Kuntze) (Terra & Viera 2019) is an edible fruit, has a low sugar (fructose, glucose and sucrose) and lipid content and is rich in fiber, minerals (phosphorus, magnesium, calcium, copper and zinc), antioxidants (anthocyanins, carotenoids, phenolics and lycopene) and vitamins (B_6, C and E) (Diep et al. 2020; Nascimento et al. 2016; García et al. 2018).

Some authors suggest that UFP can control variables related to heath and diseases prevention. However, published studies on this subject are still scarce, and no systematic review on this topic has been identified. Thus, we intend to critically analyze the studies on ora-pro-nobis and *tamarillo* in order to verify their efficacy and applicability to control these variables. In the case of studies involving rats, we estimated the human equivalent dose to be ingested and that could lead to similar effects.

In the methodology section, we detail how the search in the databases and selection of included studies was carried out, according to the Prisma protocol. In the results section, we present the studies that had health outcomes with the use of ora-pro-nobis and *tamarillo*, their characteristics, main results and the analysis of the risk of bias. In the discussion and conclusion sections we discuss the main health outcomes found with the routine consumption of these plants.

2 METHODS

This systematic review was conducted using the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 checklist (Page et al. 2021) and the Joanna Briggs 2020 handbook (Joanna Briggs Institute, 2020). In the review process, we based ourselves on the guiding question "Which health indicators are affected by the consumption of ora-pro-nobis and tamarillo?" and the acronym Population, Intervention, Comparison, Outcome, Study (PICOS): "P" (female and/or male) human, rodents participants and *in vitro*; "I" intervention, with clinical or experimental studies on the effects of ora-pro-nobis (*Pereskia aculeata*) and *tamarillo* (*Solanum betaceum*); "C" comparison by means of control treatment with placebo, "O" Outcome (results) with variables related to lipid and glycemic control, body composition and weight, antioxidant activity, gastrointestinal changes, neurological and antinociceptive effects, and food intake; "S" study types primarily randomized crossover, double-blind, non-randomized clinical trials, in addition to animal and *in vitro* studies.

2.1 Protocol and registration

This review protocol and registration was performed on the Open Science Work platform (OSF - https://osf.io/), under the DOI number: 10.17605/OSF.IO/DEP89.

2.2 Search strategy

Four databases (Pubmed, Cochrane, Embase and Web of Science) were searched on April 04, 2024, using compiled terms that include PICOS, and Boolean operators "AND" / "OR" (Table 1).

2.3 Studies selection

After searching the databases, the analysis of the studies and the removal of duplicates was done in the Rayyan online program. Blind analysis of the articles titles and abstracts was performed blindly by two authors (RSF, NSB). In case of divergence in the classification, a third author (VNM) participated in the final decision. All authors read the full articles.

Clinical and observational studies, human (men and women), rodents, or in vitro trials presenting health outcomes were included. Exclusion criteria were: study type (protocol, review and qualitative studies), other outcomes or study topic (other plant species, besides botanical, bromatological, physicochemical, pharmacological or food technology studies) (Fig. 1).

Table 1 – Search strategy in the databases

(To be continued)

BASES	SEARCH STRATEGY
EMBASE	('pereskia aculeata' OR 'cactus pereskia' OR 'ora pro nóbis' OR 'ora-pro-nóbis' OR 'ora-pro-nobis' OR 'ora pro nobis' OR 'solanum betaceum' OR 'cyphomandra betacea' OR 'cyphomandra crassifólia' OR '*tamarillo*' OR 'tamarilo') AND ('noncommunicable disease' OR 'non-infectious diseases' OR 'non infectious diseases' OR 'non-infectious disease' OR 'non-communicable diseases' OR 'non communicable diseases' OR 'noninfectious diseases' OR 'noninfectious disease' OR 'non-communicable chronic disease' OR 'non-communicable chronic diseases' OR 'gastrointestinal microbiota' OR 'gut microbiome' OR 'gut microbiota' OR 'gastrointestinal microbial communities' OR 'microbial community' OR 'satiety response' OR 'yy peptide' OR 'ghrelin' OR 'appetite hormone' OR 'satiety hormones' OR 'glp-1' OR 'gip' OR 'appetite regulating hormone' OR 'hunger' OR 'blood glucose' OR 'blood sugar' OR 'body weight' OR 'body weights' OR 'weight loss' OR 'weight reduction' OR 'overweight' OR 'obesity' OR 'morbid obesity' OR 'morbid obesities' OR 'grade 3 obesity' OR 'body mass index > 40' OR 'activity improved oxidative' OR 'bioactive compound' OR 'anti-oxidant capacity' OR 'nutrient' OR 'vitamin' OR 'protein' OR 'mineral' OR 'polyphenol' OR 'carotenoid' OR 'anthocyanin' OR 'anti-oxidant' OR 'nutrients' OR 'vitamins' OR 'proteins' OR 'minerals' OR 'polyphenols' OR 'anthocyanins')
PUBMED	('pereskia aculeata' OR 'cactus pereskia' OR 'ora pro nóbis' OR 'ora-pro-nóbis' OR 'ora-pro-nobis' OR 'ora pro nobis' OR 'solanum betaceum' OR 'cyphomandra betacea' OR 'cyphomandra crassifólia' OR '*tamarillo*') AND ('noncommunicable disease' OR 'non-infectious diseases' OR 'non infectious diseases' OR 'non-infectious disease' OR 'non-communicable diseases' OR 'non communicable diseases' OR 'noninfectious diseases' OR 'noninfectious disease' OR 'non-communicable chronic disease' OR 'non-communicable chronic diseases' OR 'gastrointestinal microbiota' OR 'gut microbiome' OR 'gut microbiota' OR 'gastrointestinal microbial communities' OR 'microbial community' OR 'satiety response' OR 'yy peptide' OR 'ghrelin' OR 'appetite hormone' OR 'satiety hormones' OR 'glp-1' OR 'gip' OR 'appetite regulating hormone' OR 'hunger' OR 'blood glucose' OR 'blood sugar' OR 'body weight' OR 'body weights' OR 'weight loss' OR 'weight reduction' OR 'overweight' OR 'obesity' OR 'morbid obesity' OR 'morbid obesities' OR 'grade 3 obesity' OR 'body mass index > 40' OR 'activity improved oxidative' OR 'bioactive compound' OR 'anti-oxidant capacity' OR 'nutrient' OR 'vitamin' OR 'protein' OR 'mineral' OR 'polyphenol' OR 'carotenoid' OR 'anthocyanin' OR 'anti-oxidant' OR 'nutrients' OR 'vitamins' OR 'proteins' OR 'minerals' OR 'polyphenols' OR 'anthocyanins')
Web of science	(ALL=('Pereskia aculeata' OR 'Cactus pereskia' OR 'ora-pro-nóbis' OR 'lobrobô' OR 'carne-de-pobre' OR 'Solanum bataceae' OR 'Cyphomandra betacea' OR 'Cyphomandra crassifólia' OR 'tomate-de-árvore' OR '*tamarillo*')) AND ALL=('health' OR 'functional property' OR 'health increase' OR 'benefits' OR 'noncommunicable disease' OR 'non infectious diseases' OR 'appetite hormone' OR 'overweight' OR 'obesity')

Table 1 – Search strategy in the databases

(Conclusion)

BASES	SEARCH STRATEGY
Cochrane library	‘pereskia aculeata’ OR ‘cactus pereskia’ OR ‘ora pro nóbis’ OR lobrobô OR ‘carne de pobre’ OR ‘solanum betaceum’ OR ‘cyphomandra betacea’ OR ‘cyphomandra crassifólia’ OR ‘tomate de árvore’ OR ‘tomate da índia’ OR ‘tomate francês’ OR ‘*tamarillo*’ OR ‘tamarilo’ in All Text AND ‘health’ OR ‘healthy’ OR ‘life quality’ OR ‘functional property’ OR ‘functional properties’ OR ‘benefit’ OR ‘benefits’ OR ‘beneficial property’ OR ‘beneficial properties’ OR ‘welfare’ OR ‘health improvement’ OR ‘improvements’ OR ‘well-being’ OR ‘health increase’ OR ‘recovery’ OR ‘health enhance’ OR ‘beneficial effects’ OR ‘dietary fiber’ OR ‘functional ingredient’ OR ‘gastrointestinal symptoms’ OR ‘intestinal microbiota’ OR obesity OR ‘fecal microbiota’ OR flour OR ‘type i arabinogalactan’ OR ‘highly-methoxylated homogalacturonan’ OR ‘antinociceptive effect’ OR ‘intestinal microbiota’ OR ‘obesity’ OR ‘fecal microbiota’ OR ‘functional food’ OR flour OR ‘hydrocolloids prebiotics’ OR ‘in vitro fermentation’ OR ‘fluorescent in situ hybridisation’ OR ‘short chain fatty acids’ OR ‘increased acetylcholinesterase’ OR ‘activity improved oxidative’ OR ‘Bioactive compound’ OR ‘anti-oxidant capacity’ OR ‘nutrient’ OR ‘vitamin’ OR ‘protein’ OR ‘mineral’ OR ‘polyphenol’ OR ‘antinutritional factor’ OR ‘tannin’ OR ‘trypsin inhibitor’ OR ‘oxalate’ OR ‘carotenoid’ OR ‘lycopene’ OR ‘anthocyanin’ OR ‘anti-oxidant’ OR ‘capacity’ OR ‘nutrients’ OR ‘vitamins’ OR ‘proteins’ OR ‘minerals’ OR ‘polyphenols’ OR ‘antinutritional factors’ OR ‘tannin’ OR ‘trypsin inhibitor’ OR ‘oxalate’ OR ‘carotenoids’ OR ‘lycopene’ OR ‘anthocyanins’ in All Text - (Word variations have been searched)

Source: Organized by the authors (2024)

2.4 Risk of bias

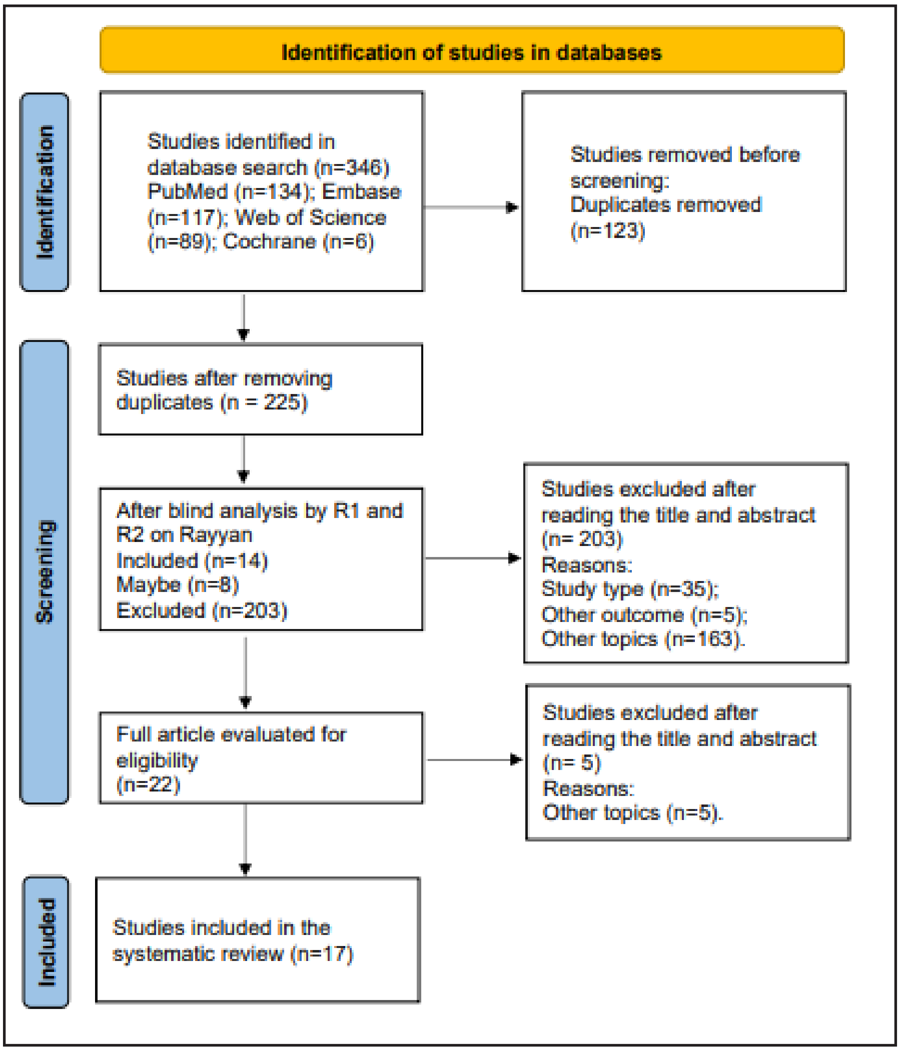
The Joanna Briggs Institute method (JBI 2020) was adopted to classify the selected studies according to the risk of bias presented. Specific questionnaires for randomized and non-randomized studies were blindly applied. For each question presented, two authors selected one of the answers “Yes, No, Confusing or Not applicable”. In case of disagreement, two other authors participated in the final decision. The total number of answers with “yes” was multiplied by 100 and divided by the total number of questions, thus classifying the study as high (>70%), moderate (50 to 69%), or low (<50%) risk (Table 3 and supplementary tables S1, S2 and S3).

3 RESULTS

3.1 Studies selection

We identified 346 articles in the databases searched. After removing duplicates and analyzing titles and abstracts, 17 articles were included. After the entire reading of the articles, we included two additional articles, which had been initially identified as potential articles to be included. Thus, 17 studies were included in this review (Figure 1).

Figure 1 – Flowchart of the selected articles for the study



Source: Authorship (2024)

3.2 Description of included studies

The selected studies were published between 2015 and 2022. In terms of the 17 articles included, ora-pro-nobis (2 with humans, 3 with animals and 1 *in vitro*) was the adopted intervention in 6 and *tamarillo* (3 with humans, 5 with animals and 3 in vitro) in 11 articles. Regarding the type of study, 9 are animal studies, 2 prospective studies with a control group, 1 adopted cross-intervention and 1 prospective study without a control group and 4 in vitro studies with gastroduodenal digestion was simulated (Table 2). As for randomization, 7 studies are randomized controlled trials and 5 are non-randomized studies (Table 2).

The main outcomes observed after the consumption of tamarillo were: reduction of total cholesterol, low-density lipoprotein (LDL), glycemia, tumor necrosis factor-alpha (TNF-α), interleukin 6, α-glucosidase, α-amylase and lipase; increase in high-density lipoprotein (HDL), total antioxidant capacity and glucose adsorption/absorption/diffusion, superoxide dismutase, acetylcholinesterase, brain-derived neurotrophic factor, reduced memory impairment; inhibition of abdominal constrictions (induced with acetic acid and formalin); and anticarcinogenic action. The consumption of ora pro-nobis resulted in: reduction of weight, visceral fat, Lee index, total cholesterol, triglycerides, LDL, very low-density lipoprotein (VLDL), atherogenic index, hunger, constipation, gastrointestinal symptoms; on the other hand, increase of high-density lipoprotein cholesterol (HDL-c) and intestinal motility; and improves rheumatoid arthritis (Table 2).

Table 2 – Characteristics and main results of selected studies that evaluated the effects of ora-pro-nobis and *tamarillo* consumption in variables related to chronic diseases control

(To be continued)

Reference	Subjects	Intervention Type	Study duration	Main results
STUDIES WITH ORA-PRO-NOBIS (*Pereskia aculeata*)				
Chen et al. (2022)	*In vitro* Experimental: Healthy female rats	Mouse macrophages (RAW264.7) DEX: 10^{-4}M (control) NO expression: PEEP: 15, 30, 60 μg mL^{-1}TNF and IL6 expression: PEEP 15, 30, 60 μg mL^{-1} Protein expression.: PEEP (30 and 60 μg mL^{-1}). Control groups: 1. blank group (n=6) 2. model group - complete Freund's adjuvante (CFA) – induced rheumatoid arthristis (n=10) Treatment groups (CFA + PEEP - *P. aculeata Mill* extract with petroleum ether): 3. L-PEEP (16 mg kg^{-1}) (n=10) 4. M-PEEP (32 mg kg^{-1}) (n=10) 5. H-PEEP (64 mg kg^{-1}) (n=10) Treatment groups (CAF + DEX – Dexamethasone) 6. DEX (0.5 mg kg^{-1}) (n=10) (positive control)	Experimental: 7 days: adaptation 14 days: inflammatory response 10 days: treatment	*In vitro* (PEEP): ↓ NO expression NO (all). ↓ mRNA expression TNF-α (all) and IL-6 (30 and 60 μg mL^{-1}) ↓ p-p38, p-MK2 expression; ↑ PTT expression. (all). Experimental: M-PEEP and H-PEEP x model: improves rheumatoid arthritis ↓ swelling; IL-6, PGE_2, TNF-α, inflammation, spleen index.

Table 2 – Characteristics and main results of selected studies that evaluated the effects of ora-pro-nobis and *tamarillo* consumption in variables related to chronic diseases control

(To be continued)

Reference	Subjects	Intervention Type	Study duration	Main results
STUDIES WITH ORA-PRO-NOBIS (*Pereskia aculeata*)				
Brasil et al. (2020)	Male *Wistar* rats	Sessions 1. obesity Induction 2. Cactus juice ingestion Control groups: 1. Hypercaloric diet (n=6) 2. Monosodium glutamate (1x/ week subcutaneous injections) (n=6) Treatment groups (subcutaneous glutamate injections, followed by 3 types of *Pereskia* juice): 1. *P. aculeata* (n=6) 2. *P. bleo* (n=6) 3. *P. grandifolia* (n=6) Leaf juice 90% water 10% leaves (1 mL twice a week)	8 weeks in each session	*P. grandifolia* juice: - ↓ food intake and total weight gain. *P. aculeata* juice x control: - Body weight, weight gain, BMI, Lee index, food intake, liver weight, hepatosomatic index remained constant.
Vieira et al. (2020)	Women	Two groups: 1. Control (n=10): drink without ora-pro-nobis flour 2. Intervention (n=12): drink containing 10g of ora-pro-nobis flour	Six weeks	Ora-pro-nobis: - ↓ body weight, waist circumference, body fat, eructation, constipation - ↑ satiety - Improved stool consistency

Table 2 – Characteristics and main results of selected studies that evaluated the effects of ora-pro-nobis and *tamarillo* consumption in variables related to chronic diseases control

(To be continued)

Reference	Subjects	Intervention Type	Study duration	Main results
		STUDIES WITH ORA-PRO-NOBIS (*Pereskia aculeata*)		
Vieira et al. (2019)	Overweight men	Groups: Treatment: 1 cookie portion with 10 g ora-pro-nobis flour/day (n=5) Control: 1 cookie portion without ora-pro-nobis flour (n=4)	6 weeks in each group; 2 weeks of washout	Treatment: - ↓ hunger, flatulence, gastrointestinal symptoms - ↑ satiety, borborygmus
Silva et al. (2017)	Female wistar rats	Single administration of dry extract of P. aculeata /kg of weight. Groups: G1: 0mg (n=6) G2: 1250 mg (n=6) G3:2500 mg (n=6) G4:5000 mg (n=6)	14 days	*P. aculeata* did not cause symptoms of acute toxicity in either group after clinical evaluation and histopathological analysis
Barbalho et al. (2016)	*Wistar* rats	Five groups 1. Commercial feed (Control) (n=10) 2. Feed with 30% ora-pro-nobis flour and 70% commercial feed. (n=10) Intestinal motility treatments: 3. Propylene glycol (Control) (n=10) 4. Cassia angustifolia (senne) and propylene glycol suspension (n=10) 5. Suspension with 30% ora-pro-nobis flour, propylene glycol. (n=10)	40 days	Ora-pro-nobis flour group: - ↓ weight gain, visceral fat, Lee index, total cholesterol, triglycerides, LDL, VLDL and atherogenic index - ↑ HDL-c, intestinal motility

Table 2 – Characteristics and main results of selected studies that evaluated the effects of ora-pro-nobis and *tamarillo* consumption in variables related to chronic diseases control

(To be continued)

Reference	Subjects	Intervention Type	Study duration	Main results
		STUDIES WITH *TAMARILLO* (*Solanum betaceum*)		
Muliarta et al. (2020)	Farmers exposed to pesticides	Two groups: 1. 250 mL of *tamarillo* juice (n=13) 2. No juice (control) (n=19)	Two weeks	*Tamarillo* Juice: - ↓ malondialdehyde - ↑ superoxide dismutase and acetylcholinesterase
Orqueda et al. (2020)	*In vitro* gastroduodenal digestion simulation	Enzyme inhibition assays with polyphenolic enriched extracts (EEP) of red *tamarillo* (seed, pulp and powder): α-glucosidase inhibition Treatment: EEP (2.5–20 μg mL^{-1}) Control: orlistat α-amylase inhibition Treatment: EEP (5–40 μg GAE mL^{-1}) Control: acarbose Lipase inhibition Treatment: EPP (2.5-20 μg mL^{-1}) Control: orlistat Glucose adsorption capacity of *tamarillo* powder 0.5 g *tamarillo* pulp, seed or skin powder + 10 mL of glucose solution (20 mM) Glucose diffusion Treatment: 0.25, 0.5 and 1g *tamarillo* powder (pulp, skin and seeds) + 5 mL of a glucose solution (20 mM) dialyzed against 40 mL of distilled water at 37 °C Control: no *tamarillo* powder Glucose ingestion by Saccharomyces cerevisiae cells Treatment: 100 μL at 10% (v/v) Saccharomyces cerevisiae suspension + EEP (10–100 mg mL^{-1}) + 1 mL glucose solution (20 mM) Control: without EEP	Not informed	All treatments: - Strong correlation between total phenolic content and inhibitory capacity of α-glucosidase, α-amylase and lipase enzymes. - Significant correlations: between seed and pulp EPP on α-glucosidase and lipase. Seeds powder x pulp and skin powders: - ↑ glucose adsorption capacity All treatments x control: - ↓ glucose diffusion rate Treatment x control (yeast): - ↑ glucose uptake by yeast cells

Table 2 – Characteristics and main results of selected studies that evaluated the effects of ora-pro-nobis and *tamarillo* consumption in variables related to chronic diseases control

(To be continued)

Reference	Subjects	Intervention Type	Study duration	Main results
STUDIES WITH *TAMARILLO* (*Solanum betaceum*)				
Khaerunnisa et al. (2019)	Albino male rats	Groups: 1. Negative control: Exposure to smoke from 3 cigarettes/day (n= 6 to 8 rats per group): 2. Positive control and exposure to cigarette smoke (n= 6 to 8 rats per group) 3. Smoke and ethanolic extract of *S. betaceum* (100 mg / kg of weight) (n= 6 to 8 rats per group) 4. Smoke and ethanol extract of *S. betaceum* (200 mg / kg of weight) (n= 6 to 8 rats per group) 5. Smoke and ethanol extract of *S. betaceum* (400 mg / kg of weight) (n= 6 to 8 rats per group)	28 days	*S. betaceum* ethanol extract: - ↑ brain-derived neurotrophic factor, c_AMP response element, memory. - ↑ transcription factor CREB, neurotrophic factors BDNF, neurons and glial cells. - ↓ memory impairment.
Asih et al. (2018)	Male wistar rats	Ethanol extract or extract of flavonoid glycosides of n-butanol extracted from *Tamarillo*, associated with maximum physical activity (swimming for 90 minutes). Treatments: 1. Control: standard diet (n=7); 2. Intense exercise (n=7); 3. 50 mg kg^{-1} Ethanol extract + intense exercise (n=7); 4. 50 mg kg^{-1} n-butanol flavonoid glycoside extract + intense exercise (n=7).	5 days	Treatment groups 3 and 450 mg kg^{-1} Ethanol extract/n-butanol flavonoid glycosides + exercise: ↓ Malondialdehyde. - ↑ activity of Superoxide Dismutase

Table 2 – Characteristics and main results of selected studies that evaluated the effects of ora-pro-nobis and *tamarillo* consumption in variables related to chronic diseases control

(To be continued)

Reference	Subjects	Intervention Type	Study duration	Main results
STUDIES WITH *TAMARILLO* (*Solanum betaceum*)				
Orqueda et al. (2017)	*In vitro* gastroduodenal digestion simulation	Salivary and gastric digestion: extracts with polyphenols from yellow *Solanum betaceum*, Argentinian seed powder, pulp and skin (4 mg GAE) + 6 mL artificial saliva + KSCN [20 g/L] + NaH2 PO4 [88.8 g / L] L] + Na2SO4 [57.0 g/L] + NaCl [175.3 g/L] + NaHCO3 [84.7 g/L] + urea [25.0 g/L] + α-amylase [48 .3 mg mL^{-1}]). Gastric digestion: pepsin (14,800 U) Pancreatic digestion: pancreatin (8 mg mL^{-1}) + bile salts (50 mg mL^{-1})	Not informed	Phenolic enriched extract of seeds, bark, and pulp: - ↑ inhibition of α-amylase and α-glucosidase Phenolic Seed Extract: - ↑ Lipase inhibition compared to pulp and skin extract All extracts: - Ability to protect red blood cells from oxidative hemolysis - ↑ antioxidant activity
Sihombing et al. (2017)	Male rats (*Mus musculus*)	5 groups Control: distilled water + normal diet (n=5) IV: 42 mg kg^{-1}.pv of methanolic extract of *tamarillo* bark (*Solanum betaceum*) + normal diet (n=5) Groups II (n=5), III (n=5) and V (n=5): extract from other plants.	Not informed	Group IV x control: - ↓ blood glucose
Salazar-Lugo et al. (2016)	Adults	Treatment: 1 juice portion with 100 g of *tamarillo* (*Solanum betaceum*)/day daily (n=54) No control group	6 weeks	- ↓ cholesterol, LDL, glycemia

Table 2 – Characteristics and main results of selected studies that evaluated the effects of ora-pro-nobis and *tamarillo* consumption in variables related to chronic diseases control

(To be continued)

Reference	Subjects	Intervention Type	Study duration	Main results
		STUDIES WITH *TAMARILLO* (*Solanum betaceum*)		
Mutalib et al, 2016	*In vitro*	Cytotoxicity assay: human tumour cell lines HepG2 (liver), MDA-MB-231(breast) and 3T3 (normal mouse fibroblast) Treatment: *Solanum betaceum* 1 mg mL^{-1} of DMSO (6.25, 12.5, 25, 50, 100, 200 µg mL^{-1}). Positive control: doxorubicin (0.20, 0.39, 0.78, 1.56, 3.13, 6.25, 12.5, 25 µg mL^{-1}) Negative control: culture medium (1% DMSO - dimethyl sulfoxide)	Once	*S. betaceum*: Inhibition: proliferation of HepG2 and MDA-MB-231 cell lines; maintained the viability of healthy cellsDoxorubicin: ↑ inibition human tumour and normal cells.
Nascimento et al. (2015)	Female Swiss mice (25-35 g)	Induction of abdominal constrictions with acetic acid (0.6%, 0.45 mL/mouse) and nociception with formalin (20 µl of a 2,5%) Control VEH – vehicle (saline, 10 mL kg^{-1}) (n = 4 to 6) Treatment: 50E- type I arabinogalactan purified (Pectic polysaccharides from pulp of the *Tamarillo* - *Solanum betaceum*): 0,1 mg/ Kg 50E (n = 4 to 6) 1 mg/ Kg 50E (n = 4 to 6) 10 mg/ Kg 50E (n = 4 to 6) 100 mg/ Kg 50E (n = 4 to 6 animals per group)	Once	Treatment 50E 1, 10, 100 mg/ Kg: - Inhibition: abdominal constrictions - NS: nociception formalin test

Table 2 – Characteristics and main results of selected studies that evaluated the effects of ora-pro-nobis and *tamarillo* consumption in variables related to chronic diseases control

(Conclusion)

Reference	Subjects	Intervention Type	Study duration	Main results
		STUDIES WITH *TAMARILLO* (*Solanum betaceum*)		
Abdul Kadir, Rahmat & Jaafar (2015)	Adult male rats (*Sprague-Dawley*)	Five groups: *Tamarillo* groups: (*Solanum betaceum*) extract dosages: 1. Low (150mg kg−1) (TLDG) (n=8) 2.Medium (200mg kg − 1) (TMDG) (n=8) 3. High (300mg kg −1) (THDG) (n=8) Control Groups: 1. Negative control (NC): normal weight rats - normal diet + distilled water (n=8) 2. Positive control (PC): obese rats – high fat diet + distilled water (n=8)	Obesity induction: 10 weeks Treatments: 7 weeks.	TLDG, TMDG and THDG X NC and PC: - ↓ total cholesterol, TNF-α, IL-6 - ↑ HDL-C and total antioxidant capacity
Nascimento et al. (2013)	Female Swiss mice	Induction of abdominal constrictions with acetic acid and formalin Treatment: 1.- STK-1000R (galactoarabinoglucuronoxylans, alkaline fraction extracted from *tamarillo*) (n = 6 to 8 animals per group) 2. – Nociception (formalin) (n = 6 to 8 animals per group)	Once	STK-1000R: - Inhibition of abdominal constrictions

Source: Organized by the authors (2024). Note: EEP – Extract enriched with polyphenols; HDL – high-density lipoprotein; HDL-c - high-density lipoprotein cholesterol; H-PEEP – high content of petroleum ether extract with Pereskia aculeata; KSCN - Potassium thiocyanate; LDL - low-density lipoprotein; L-PEEP – low content of petroleum ether extract with Pereskia aculeata; M-PEEP – medium content of petroleum ether extract with Pereskia aculeata; NC – Negative control; PC - Positive control; PEEP – Pereskia aculeata extract with petroleum ether; TNF-α - tumor necrosis factor-alpha; VLDL - very low-density lipoprotein

3.3 Risk of bias assessment

Almost all studies (14/17) had a low, 2 moderate and 1 high risk of bias (Table 3 and supplementary tables S1, S2 and S3). The main weaknesses were the participants blinding allocation and data analyses, there was incomplete follow-up in 1 study. Clear indication of cause-and-effect relationship, similarity of the participants characteristics presented in the treatment groups, use of adequate methods to evaluate the results and statistical analyses of the data are the strengths presented by the studies (Table 3 and supplementary tables S1, S2 and S3).

4 DISCUSSION

As far as we know, this is the first systematic review involving humans, animals, and in vitro studies in which the effect of ora-pro-nobis or *tamarillo* on variables related to chronic non-communicable diseases was evaluated. The effects of the ingestion of these plants are presented below (Table 2).

4.1 Effects on lipid profile, antioxidant and anti-inflammatory activity

Both plants exerted positive effects on the lipid profile in humans (Salazar-Lugo et al. 2016; Abdul-Kadir, Rahmat & Jaafar 2015) and in animals (Barbalho et al. 2016). That effect may be attributed, at least in part, to the viscosity of the fibers present in these plants. Both are rich in soluble fibers capable of inducing the elimination of bile acid in the feces, reducing the concentration of serum cholesterol, mainly of LDL (Chutkan et al. 2012).

Table 3 – Selected studies bias risk

(To be continued)

Reference	Bias risk	Risk percentagem
Chen et al. (2022) [b]	Low	(88%)
Brasil et al. (2020) [b]	Low	(100%)
Muliarta et al. (2020) [a]	Low	(88%)
Orqueda et al. (2020) [c]	Low	(100%)
Vieira et al. (2020) [a]	Low	(100%)
Vieira et al. (2019) [a]	Moderate	(66,66%)
Khaerunnisa et al. (2019) [b]	Low	(77,77%)
Asih et al. (2018) [a]	Low	(72,72%)
Silva et al. (2017) [a]	Low	(75%)
Orqueda et al. (2017) [c]	Low	(100%)
Sihombing et al. (2017) [b]	Low	(100%)
Mutalib et al, 2016 [c]	Low	(100%)
Barbalho et al. (2016) [a]	High	(45,45%)

Table 3 – Selected studies bias risk

(Conclusion)

Reference	Bias risk	Risk percentagem
Salazar-Lugo et al. (2016) [b]	Low	(85,71%)
Abdul-Kadir et al. (2015) [a]	Low	(72,72%)
Nascimento et al. (2015) [b]	Low	(100%)
Nascimento et al. (2013) [b]	Moderate	(66,66%)

Source: Organized by the authors (2024). [a] Bias Risk of Randomized Trials Selected by Joanna Briggs. [b] Bias Risk of non-randomized studies selected by Joanna Briggs. [c] Bias Risk from in vitro studies, adapted from the Joanna Briggs Handbook's checklist of non-randomized studies

Flavonoid glycosides present in *tamarillo* are capable of increasing superoxide dismutase (SOD) enzymes activity. This effect occurs directly when a hydroxyl group allows flavonoids to scavenge free radicals, donating hydrogen atoms, preventing the formation of reactive oxygen species (ROS). As a result, they indirectly increase endogenous antioxidant genes expression, resulting in SOD enzyme synthesis increase. In addition, they break the chain of fat peroxidation. An increase in free radicals can be caused by reactions with unsaturated fatty acids (LH), forming carbon (L) radicals in the form of free fat, which in turn react with oxygen to form peroxyl radicals (LOO). If the peroxyl radical reacts again with the other unsaturated fatty acids, cytotoxic lipid hydroperoxide (LOOH) and free fatty acid (L) are formed, so that a chain reaction occurs. The reaction will end if free fat is formed in the initiation stage or other radicals formed in the propagation stage react back with the other radicals in non-radical products (Raka et al. 2018).

The increase in enzymes such as superoxide dismutase (SOD) in the circulation may be related to the antioxidant action mechanism of bioactive compounds, which is not limited to the elimination of free radicals, since it includes the regulation of antioxidant enzymes, detoxification, metabolic modulation and of gene expression (Eberhardt & Jeffery 2006). Consumption of *tamarillo* reduced the concentrations of malondialdehyde and increased SOD in studies with serum samples in humans (Muliarta et al. 2020) and in the liver tissue of rats (Raka et al. 2018).

Phenolic compounds, including the anthocyanins present in *tamarillo*, inhibit in vitro LDL oxidation and protect PC12 neuronal cells from damage induced by oxidative stress. This effect is attributed to its free radical scavenging activity, suggesting that consuming this food can prevent atherosclerosis (Raka et al. 2018). *Tamarillo* also contains a high content of rosmarinic acid, which is a polyphenol with anti-inflammatory, antibacterial, antidepressant, antiviral, anticarcinogenic and chemoprotective properties. Under hyperlipidemia and hyperglycemia oxidative stress conditions, rosmarinic acid protects pancreatic tissue from glucolipotoxicity or activates antioxidant enzymes in tissues such as the liver, kidney and other organs sensitive to lipid peroxidation. Therefore, rosmarinic acid can act synergistically with other polyphenols and carotenoids, reducing lipemia, especially in individuals with altered lipid profile (Salazar-Lugo et al. 2016).

Consumption of at least 150 mg kg-1 of *tamarillo* for 7 weeks reduced the pro-inflammatory cytokines TNF-α and IL-6 and increased total antioxidant capacity in animals (Abdul Kadir et al. 2015). These results are interesting and make us wonder whether these same effects would be observed in humans. To evaluate such effect, we need to estimate the dose to be tested in humans. Therefore, we can extrapolate the dose tested in animals to the dose in humans as a body surface area normalization function (Reagan-Shaw et al. 2008). Thus, we multiply the established dose in rats (150 mg kg-1) by the constant (Km = 3) for rats and then divide by the constant (Km = 37) for humans. Therefore, the human equivalent dose would correspond to approximately 12.2 mg kg-1, which corresponds to 732 mg considering a person weighing 60 kg.

Tamarillo seeds have high unsaturated fat content, while the skin outer part contains protein, and the inner part has higher contents of phenols, dietary fiber and water (Martin et al. 2021).

In a simulated digestion study, the authors verified that the *tamarillo* powder presented ascorbic acid (117.0 ± 10.2 mg AAE/100 g), phenolics (31 types - caffeic acid, rosmarinic acid derivatives and flavonoids), carotenoids (1.41 ± 0.09 g β-EC/100 g) and anthocyanins only in the skin (1.78 ± 0.50 C-3GE/100 g). All *tamarillo* extracts reduced the cation radical ABTS (0.8 and 1.38 μg GAE/mL) by protecting red blood cells from oxidative hemolysis. That effect was superior to commercial antioxidants. Thus, the fruit can reduce oxidative stress and the risk of developing metabolic syndrome, as well as diseases such as diabetes and obesity (Orqueda et al. 2017). The antioxidants (phenolics, pigments and ascorbic acid) inactivate the harmful effects of oxygen synthesis, preventing the action of free radicals, which promote cell death when in high concentrations, by capturing and neutralizing these compounds, enabling the treatment and preventing oxidative stress and inflammation occurrence (Demirci-Cekic et al. 2022; Lin et al. 2021; Wang & Zhu 2020).

Phenolics are antioxidants that modulate various cell survival and cell cycle genes. They exert an anti-inflammatory effect by calcium homeostasis regulation. They act on mitogen protein kinase (MAPK) signaling, protein kinase C (PKC), serine/threonine, protein kinase B (Akt/PKB) signaling, MAP kinase cascade, and phase II antioxidant detoxifying enzymes. They inhibit phosphoinositide 3-kinase (PI 3-kinase), tyrosine kinases, nuclear factor kappa B (NF-κB), transcription factor Jun (c-JUN), pro-inflammatory enzymes (cyclooxygenase-2 (COX-2) and inducible nitric oxide synthase (iNOS) by peroxisome proliferator-activated receptor gamma (PPARγ), reducing metabolic dysfunctions in obese individuals (Cianciosi et al. 2022; Garcia et al. 2019; Soobrattee et al. 2005; Williams et al. 2004).

In addition to exerting antioxidant activity (Cianciosi et al. 2022), the phenolic compounds present in *tamarillo* powder have a lipid-lowering action (Orqueda et al. 2020; Torres et al. 2021). In an in vitro study of free radical scavenging by the DPPH method, the authors also observed a strong correlation between ora-pro-nobis phenolic compounds content and the antioxidant activity (Torres et al. 2021).

Ora-pro-nobis is rich in vitamins C, total phenols (Barreira et al. 2020; Garcia et al. 2019) and α-carotene (Agostini-Costa et al. 2014; Takeiti et al. 2009). Vitamin C and carotenoids act as antioxidants, protecting cells against oxidative damage induced by free radicals (Wang et al. 2012), reducing the effects of free radicals and inflammatory processes in the body (Barbalho et al. 2016). Consumption of a diet rich in carotenoids resulted in TNF-α reduction as blood carotenoids increased in healthy subjects (Torres et al. 2021). Elevated concentrations of plasma carotenoids are associated with oxidized LDL reduction, attributing a protective role to lipophilic antioxidants against LDL lipid peroxidation (Bacchetti et al. 2019).

In other studies, involving healthy subjects, carotenoids intake was positively correlated with total dietary antioxidant capacity (Wang et al. 2012) and favorably impacted inflammation status, reducing TNF-α concentration as blood carotenoids increased (Torres et al. 2021). High concentrations of plasma carotenoids are associated with oxidized LDL reduction, attributing a protective role to lipophilic antioxidants against lipid peroxidation of LDL (Bacchetti et al. 2019).

4.2 Effect on blood glucose, body weight and body fat

Consumption of a juice containing 100 g of *tamarillo* per day reduced blood glucose in adults (Salazar-Lugo et al. 2016). In a rat study, consumption of 42 mg of *S. betaceum* (*C. betacea*) peel methanolic extract / kg of body weight also reduced blood glucose (Sihombing et al. 2017). In order to estimate the corresponding dose to be tested in humans, as a function of the body surface area normalization, we considered the dose established in rats (42 mg kg-1), besides the previously mentioned constants for rats (Km = 3) and humans (Km = 37) (Reagan-Shaw et al. 2008). Thus, the equivalent dose in humans would be 3.4 mg kg-1, which corresponds to 204 mg, considering an individual weighing 60 kg.

The polyphenolic components present in *tamarillo* extract inhibit α-glucosidase and α-amylase enzymes involved in carbohydrate metabolism, in a simulated gastroduodenal digestion study (Orqueda et al. 2017, 2020). Suppression of glucose absorption from the gastrointestinal tract may occur through the action of hypoglycemic agents, which inhibit α-glucosidase and α-amylase enzymes. Since there is a reduction in carbohydrate hydrolysis, glucose absorption is reduced, as well as postprandial blood glucose and insulin resistance, favoring the control of type 2 diabetes mellitus (Costamagna et al. 2016; Ghani 2015; Orqueda et al. 2017; Santoso et al. 2022).

In simulated gastroduodenal digestion, *tamarillo* delayed the passage of glucose through the dialysis membrane and inhibited glucose diffusion compared to control. The results of that study would be related to the reduction in the amount and access of glucose to the intestinal epithelium to be absorbed. The ability of *tamarillo* to reduce glycemia can also be attributed to fibers viscosity, which has a dual action, reducing gastric emptying rate and glucose absorption in the intestinal lumen (Costamagna et al. 2016). Thus, a lower intestine glucose absorption intestine reduces postprandial glucose and insulin serum concentrations.

Another mechanism that could explain the reduction in blood glucose would be the increase in reported cellular uptake (Orqueda et al. 2020) in a yeast model used to evaluate the mechanism of glucose transport across cell membranes. In that study, *tamarillo* increased glucose uptake by yeast cells. That effect would be exerted by the polyphenols fraction present mainly in fruit seed flours, which could favor glucose entry into the cells and decrease blood glucose (Costamagna et al. 2016). Polyphenolic components of *tamarillo* extract inhibited enzymes such as pancreatic lipase in an in vitro gastroduodenal digestion assay (Orqueda et al. 2017, 2020). Pancreatic lipase is responsible for the hydrolysis of 50 to 70% of total dietary fat, forming fatty acids that can be absorbed by the digestive system (Birari & Bhutani 2007; Orqueda et al. 2017; Zhou et al. 2021). Inhibition of that enzyme has been clinically used in obesity treatments through medications such as Orlistat. However, other inhibitors with fewer side effects still need to be identified (Birari & Bhutani 2007). Thus, the inhibition of lipase by *tamarillo* extract can reduce intestinal fatty acid absorption, favoring body weight control. In studies involving obese mice, lipase inhibition reduced body weight gain (Grove et al. 2012). Thus, *tamarillo* would be used as an alternative natural source for obesity prevention and treatment. In overweight men, ingestion of 10 g of ora-pro-nobis flour for 6 weeks reduced hunger and increased satiety (Vieira et al. 2019). Women consumption of the same amount of flour and during the same time as in the previous study increased satiety, reduced waist circumference, body fat and body weight (Vieira et al. 2020). In an animal study, the ingestion of ora-pro-nobis flour for 40 days reduced body weight gain, visceral fat and the Lee index used to assess obesity in rats (Barbalho et al. 2016).

Such effects may have occurred due to the high fiber content of that food (Barreira et al. 2020), which help to reduce gastric emptying rate and stimulate the secretion of the anorectic hormone GLP-1 (Chutkan et al. 2012), increasing satiety. In addition, ora-pro-nobis is a source of phytochemicals, such as polyphenols (Vieira et al. 2020).

We did not identify the mechanism of action of the phenolic compounds present in *tamarillo* and ora-pro-nobis. However, the authors of a systematic review indicated that there are similarities in the effects of different polyphenols. Some proposed mechanisms of action are reduced adipocyte differentiation and fatty acid synthesis, increased fatty acid oxidation, thermogenesis, energy expenditure and satiety. The limited understanding about that indicates that future research is needed to confirm *tamarillo* and ora-pro-nobis phenolic compounds mechanisms of action (Farhat et al. 2017).

In contrast, in another study involving rats, consumption for 8 weeks of different species of the plant (*Pereskia aculeata*, *Pereskia bleo)* or *Pereskia grandifolia*) maintained adipose tissue constant in the obesity-inducing stage (monosodium glutamate, sucrose and high-calorie diet). *Pereskia grandifolia* juice decreased food intake and weight gain after the 8 weeks of the study. On the other hand, body weight remained unaffected after the *P. aculeata* treatment and the control. Rats in the treatment group received 0.1 mL of ora-pro-nobis twice a week. Therefore, this amount of *P. aculeata* was insufficient to change the variables evaluated in Wistar rats (Brasil et al. 2020).

Healthy intestinal microbiota has more probiotic bacteria that produce short-chain fatty acids (SCFA) - acetic, propionic and butyric acids, which favor the maintenance intestinal cells, resulting in low permeability and anti-inflammatory effect (Liu et al. 2021; Scortichini et al. 2020). Individuals with obesity have intestinal dysbiosis, with a greater amount of pathogenic than of probiotics bacteria. This can result in enterocytes and tight junctions degradation, increased intestinal permeability, favoring the installation of an inflammatory profile. In addition, it can reduce the synthesis of Glucagon-Like Peptide 1 (GLP-1) and Peptide YY (PYY), causing satiety and hunger dysfunction, increased lipolysis and insulin resistance (Bianchi et al. 2019; Reagan-Shaw et al. 2008).

After 24 h of fermentation, *tamarillo* hydrocolloids stimulated the growth of Bifidobacteria and lactobacilli - beneficial bacteria, and the production of SCFA such as acetate, propionate and butyrate, showing prebiotic potential (Gannasin et al. 2015). Thus, it is possible that the effect of these UFP on blood glucose and body weight verified in the studies presented above is also related to their impact on the intestinal microbiota.

4.3 Gastrointestinal effects

Ora-pro-nobis is rich in dietary fiber, which promotes improvement in gastrointestinal symptoms, increases fecal volume, decreases pH in the digestive tract and reduces intestinal transit time (Vieira et al. 2020). Ora-pro-nobis consumption for 40 days increased intestinal motility in rats (Barbalho et al. 2016). A drink with 10 g of ora-pro-nobis flour reduced constipation and improved stool consistency in women (Vieira et al. 2020), besides reducing gastrointestinal symptoms and flatulence in men (Vieira et al. 2019). Ora-pro-nobis is rich in dietary fiber, which improves gastrointestinal symptoms, increases fecal volume, decreases pH in the digestive tract and reduces intestinal transit time (Vieira et al. 2020). In mice, *tamarillo* inhibited abdominal constrictions due to galactoarabinoglucuronoxylan present in *tamarillo* pulp, which promotes analgesic effects through anti-inflammatory mechanisms (Nascimento et al. 2015, 2016).

There is a lack of human or animal model studies investigating gastrointestinal outcomes in response to *tamarillo* ingestion. In an in vitro study, seed mucilage and *tamarillo* pulp hydrocolloids were resistant to digestive enzymes. Once fermented by the intestinal microbiota, the researchers identified the formation of different short-chain fatty acids types, which stimulated the growth of beneficial bacteria and suppressed the proliferation of some pathogenic bacteria (Nascimento et al. 2013). Due to its in vitro prebiotic properties, *tamarillo* hydrocolloids present three main characteristics: resistance to digestion (acidity and digestive enzymes), short-chain fatty acids formation during fermentation, growth of beneficial gut bacteria, and suppression of the ones considered pathogenic (Gannasin et al. 2015).

4.4 Other potential effects

Solanum betaceum is a promising anticancer agent, with a reduction in the proliferation of cancer cells (liver and breast), without exerting cytotoxic effects in healthy cells 3T3 (CI50 > 200,00 μg mL^{-1}). Cancer prevention may be due to several bioactive compounds. In the case of *tamarillo*, phenolic compounds stand out in that matter (Mutalib et al. 2016). Khaerunnisa et al. (2019) found an increase in neurotrophic factor and memory improvement. However, the neuroprotective effect of *tamarillo* after smoking impairment memory in albino rats, after the consumption of *tamarillo* for 28 days. In an in vitro study, the protective effect of phenolic compounds present in *tamarillo* on PC12 neuronal cells against damage induced by oxidative stress was identified (Kou et al. 2009).

Tamarillo has also been associated with increased neurotrophic factors, thus increasing glial cell activation to protect brain cell damage, and prevent memory impairment in the case of exposure of rats to cigarette smoke (Khaerunnisa et al. 2019). There is a lack of studies investigating the effect of *tamarillo* on neurodegenerative diseases.

The antitumor effects of *tamarillo* should also be explored, since the polysaccharides present in that food showed apoptotic characteristics on different cancer cell lines in vitro, which indicates its antitumor potential (Kumar et al. 2016).

Furthermore, it is suggested that galactoarabinoglucuronoxylan present in *tamarillo* pulp promotes analgesic effects through anti-inflammatory mechanisms (Nascimento et al. 2016; Pinto et al. 2015). Arabinogalactan type 1 is a pectic polysaccharide extracted from *tamarillo* pulp. In a study with female swiss mice, the consumption of 1-100 mg kg^{-1} inhibited abdominal constrictions induced by acetic acid (Nascimento et al. 2015). In humans, that dose would be equivalent to 0.08 mg kg-1, which corresponds to 4.86 mg in an individual weighing 60 kg, considering that constants previously indicate (Reagan-Shaw et al. 2008).

The OH elimination capacity of the *Pereskia* extracts was correlated ($p \leq 0.05$) to its phenolic compounds ($r = 0.8537$), flavonoids ($r = 0.8112$), proteins ($r = 0.8112$) and caffeic acid ($r = 0.8365$) contents. Besides these compounds strongly correlated with the antioxidant activity, measured by DPPH, FRAP and Cu2+ methods (Cruz et al. 2021). In vitro the maximum administered dose of extract of *Pereskia* (PEEP) 60 ug/mL, maintained cell viability, reduced the expression of inflammatory markers, and apparently regulated the p38/MAPK anti-inflammatory signaling pathway by reducing the expression of p-p38, p-MK2 and increasing the expression of PTT. In rats, consumption of 32 and 64 mg kg^{-1} PEEP/kg of body weight improves rheumatoid arthritis, by reduces foot swelling, spleen index, bone surface erosion and joint space narrowing; reduce the formation of synovial cells, inflammatory cells and pannus in the foot and ankle joints and reduces the secretion of TNF-α, IL-6, PGE2 in the serum of mice, decreases the expression of p-p38 and p-MK2 in the ankle joint and reduces PTT phosphorylation, reduced inflammatory indicators (Chen et al. 2022). To estimate the corresponding dose to be tested in humans, as a function of body surface normalization, we once again considered the dose established in rats (32 and 64 mg kg^{-1}), the constant for rats (Km = 3) and for humans (Km = 37) (Reagan-Shaw et al. 2008).

Thus, the equivalent dose in humans would be 2.6 and 5.2 mg kg^{-1}, which corresponds to 155.7 and 311.4 mg in an individual weighing 60 kg.

4.5 Strengths and limitations

As far as we know, this is the first systematic review to analyze studies in which the effect of ora-pro-nobis or *tamarillo* on variables related to chronic non-communicable diseases was evaluated. Most of the studies selected for this review had a low risk of bias, thus increasing the reliability of the results reported here. However, the scarce number of studies on this subject, the types of intervention, the ways of consumption and quantities tested in these studies are quite heterogeneous. In one of the studies (Vieira et al. 2019), there was a high participant dropout, which was not replaced and without indicating the reasons why the participants were unable to complete the protocol (Vieira et al. 2019). That type of information would be useful when designing future studies on that topic.

Despite these limitations, the results of the studies available to date suggest the positive effect of these UFP on the lipid, glycemic and inflammatory profile; antioxidant capacity, appetite, satiety, anthropometric measurements, body fat, gastrointestinal symptoms and memory. Daily consumption of ora-pro-nobis from 100 g of fresh leaves or 10 g of flour promoted an improvement in health indicators, as evidenced in studies (Vieira et al. 2019, 2020). There was a positive health outcome evidenced in studies by Salazar-Lugo et al. (2016) and Muliarta et al. (2020), with daily consumption starting at 100 g of fresh *tamarillo*. These recommended dosages are feasible in clinical practice, and equivalent to the food pyramid recommendation (Philippi et al. 1999). However, well-designed clinical studies must be conducted to identify the amounts and time in which these plants must be ingested to result in the control of chronic non-communicable diseases in humans.

The safety of consumption of these UFP should also be evaluated in these studies. We identified in the literature only one study in which this aspect was addressed. In that study, the authors verified no toxic symptoms in rats that received up to 5000 mg kg^{-1} of ora-pro-nobis per day for 14 days, which would be equivalent to 385 g of fresh leaves per day (Silva et al. 2017). Converting again that amount to the amount estimated as safe for humans (Reagan-Shaw et al. 2008), we could consider that 405.4 mg kg^{-1} of the plant could be safely ingested by humans. Similarly, future animal studies should evaluate the safety of *tamarillo* ingestion. It would be interesting to further investigate the effect of different species and parts of these UFP, due to their heterogeneous composition (Martin et al. 2021).

5 CONCLUSION

Ora-pro-nobis and *tamarillo* exert beneficial effects on the lipid profile. While ora-pro-nobis reduces food intake, anthropometric measurements of body fat, gastrointestinal symptoms and improves rheumatoid arthritis, *tamarillo* contributes to control glycemia, reduces inflammation, increases antioxidant capacity, reduces memory impairment and anticarcinogenic action. To improve these health indicators, we suggest consuming 100 g of fresh leaves or 10 g of flour daily; and or 100 g of fresh *tamarillo*. However, more future studies should be conducted to verify the amount and time in which these UFP should be ingested to promote positive effects on such variables and to control diseases like obesity, diabetes mellitus and cardiovascular diseases, without resulting in toxic effects. Such studies are essential so that their results can be applied to clinical practice and can be used in public health policies.

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