

OP-018 [Apitherapy]

Inhibitory activities of Chinese propolis on alpha-glucosidase and ended glycosylation products

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BACKGROUND: In 2030, the number of diabetic patients in the world would amount to 366 million and death related to diabetes mellitus accounts for about 9% global mortality, particularly type 2 diabetes mellitus. In treatment of type 2 diabetes, the suppression of postprandial hyperglycemia and ended glycosylation products can decrease the risk of complications.

METHODOLOGY: This study qualitatively and quantitatively analyzed the ethanol extracts of propolis (EEP) using HPLC-PDA-QTOF. Inhibitory activities of EEP against α -glucosidase were determined by using 4-nitrophenyl-D-glucopyranoside, sucrose and maltose as substrates, and acarbose as a positive reference. The inhibitory potential of various EEP on AGEs (advanced glycation end products) and oxidative modifications were investigated in bovine serum albumin (BSA)- glucose and BSA-methylglyoxal models. **RESULTS and CONCLUSIONS:** Experimental results show that Chinese propolis is a poplar-type propolis, based on its chemical composition. All EEP can effectively inhibit the activity of α -glycosidase to control postprandial hyperglycemia. The 75% EEP showed the highest inhibitory effect on-glucosidase and sucrase and were a noncompetitive inhibition mode. 50% EEP, 95%, EEP and 100% EEP exhibited a mixed inhibition mode, while water extracts of propolis (WEP) and 25% EEP demonstrated a competitive inhibition mode. All propolis extracts effectively inhibited the formation of ended glycosylation products, including total AGEs, pentosidine, and N ϵ -carboxymethyllysine. Furthermore, all EEP can effectively inhibit protein oxidative modification. Notably, 75% EEP exhibited the highest inhibitory activity, surpassing the chemical inhibitor aminoguanidine. **PRACTICAL IMPLICATIONS:** These findings provide reliable evidence supporting the potential use of poplar-type propolis as novel nutraceuticals aimed at preventing and treating diabetes.



Inhibitory Activities of Chinese Propolis on alpha-Glucosidase and Advanced Glycation End Products

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Background

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Inhibition on glucosidase

3

Inhibition on glycosylation

1 Background



- ❖ Propolis is a sticky mixture that honey bees collect resin from tree buds, leaves or wounds.
- ❖ Composed of 55% resin, 30% beeswax, 10% volatiles, 5% pollen & others.
- ❖ The annual output of Chinese propolis reaches approximately 400 tons, ranking first in the world.
- ❖ Chinese propolis comes from phenolics resins and belongs to poplar-type propolis



1 Background

Journal of Apicultural Research, 2017
<https://doi.org/10.1080/00218839.2017.1373512>



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ORIGINAL RESEARCH ARTICLE

A plant origin of Chinese propolis: *Populus canadensis* Moench

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Article

Botanical Origins and Antioxidant Activities of Two Types of Flavonoid-Rich Poplar-Type Propolis

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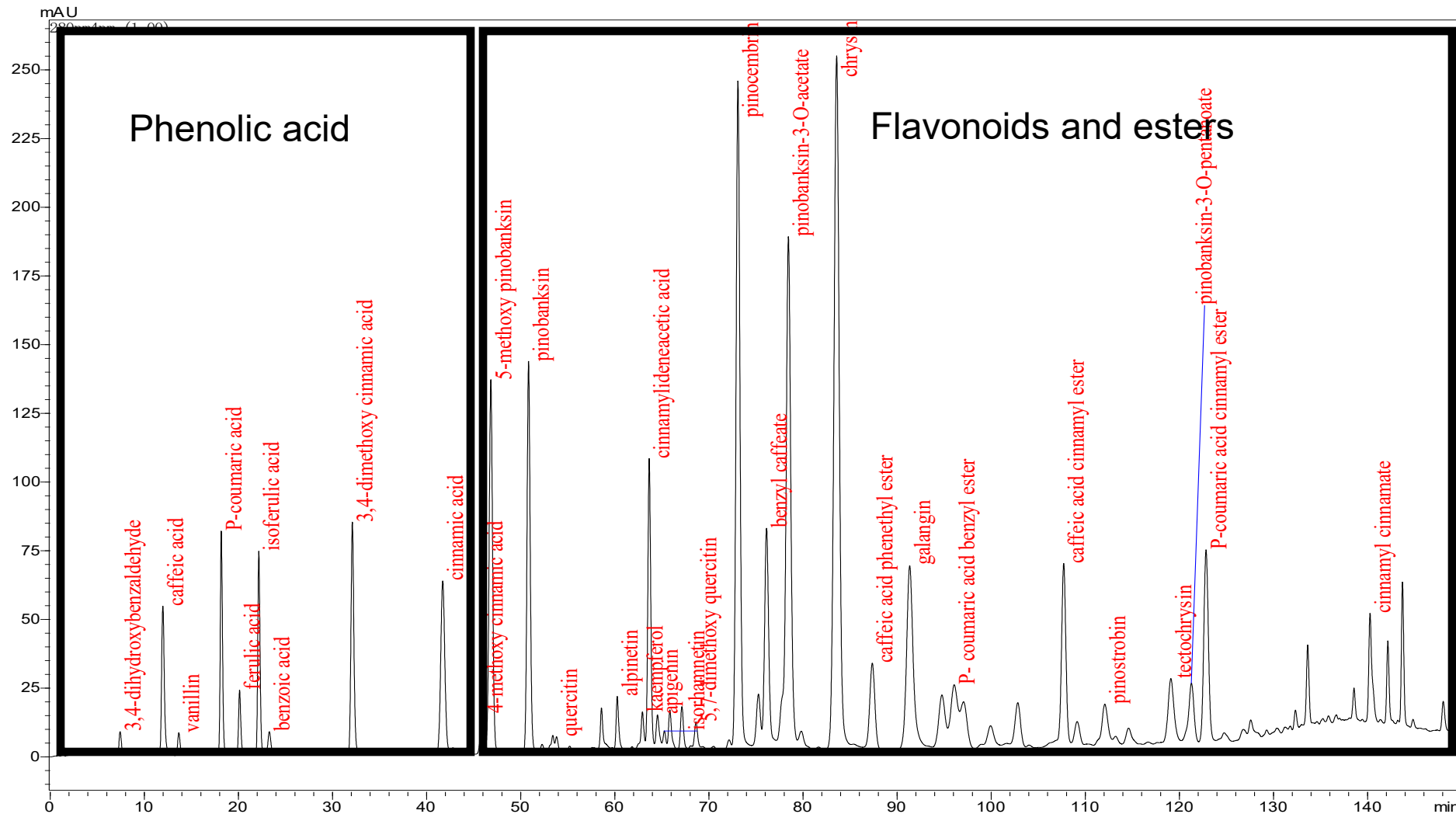
² Jiangsu Beevip Biotechnology Co., Ltd., Taizhou 225300, China

1 Background

- Chemical compound analysis

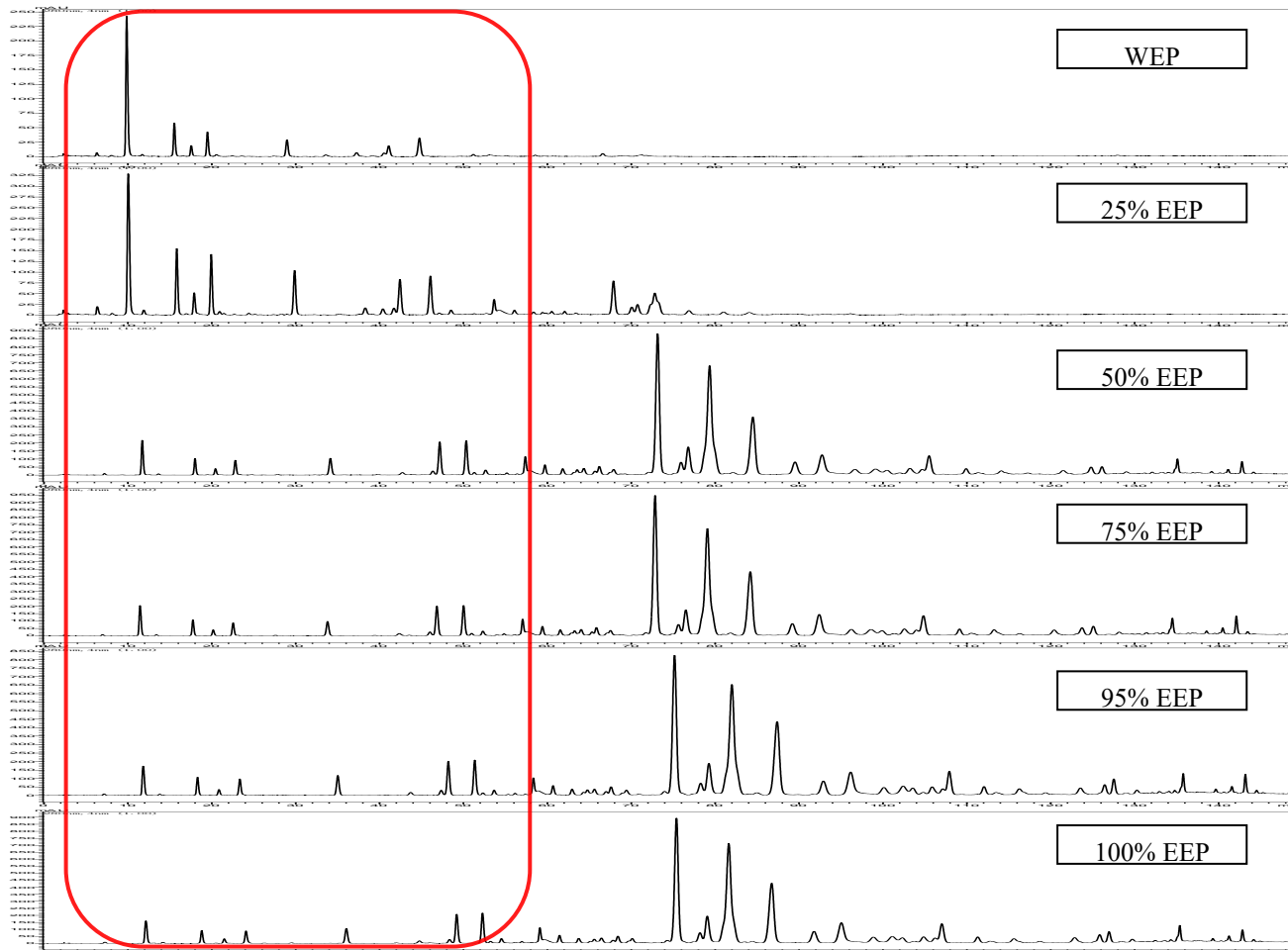
29 flavonoids

18 phenolic acid and esters



1 Background

Phenolics of Ethanol/Water Extracts



➤ WEP and 25% EEP, showed simple HPLC chromatograms with limited amount of peaks located in the region of retention times up to 50 min

➤ 75, 95, and 100% EEP presented the complex chromatograms with many peaks between the retention times of 10 and 140min.

1 Background

Phenolics of Ethanol/Water Extracts

TABLE 3: Quantitation of the constituents in different propolis extract.

Components	Content (mg/g of propolis)					
	WEP	25% EEP	50% EEP	75% EEP	95% EEP	100% EEP
3,4-Dihydroxybenzaldehyde	0.03	0.11	0.11	0.10	0.11	0.11
Vanillic acid	0.01	0.02	—	—	—	—
Caffeic acid	2.13	3.42	3.74	3.74	3.50	3.30
Vanillin	0.05	0.12	0.17	0.16	0.18	0.18
<i>p</i> -Coumaric acid	0.37	1.08	1.33	1.40	1.50	1.32
Ferulic acid	0.22	0.63	0.92	0.94	0.88	0.87
Isoferulic acid	0.46	1.66	2.20	2.08	2.60	2.42
Benzoic acid	0.54	1.09	1.08	1.06	—	—
3,4-Dimethoxycinnamic acid	0.22	0.81	1.75	1.60	2.00	1.84
Cinnamic acid	0.02	0.04	0.10	0.10	0.11	0.09
4-Methoxycinnamic acid	0.08	0.19	0.55	0.57	0.65	0.59
Cinnamylideneacetic acid	—	0.07	0.30	0.34	0.37	0.30
Benzyl caffeate	—	1.55	20.20	20.34	23.54	22.36
Phenethyl caffeate	—	0.37	10.49	10.51	12.33	11.30
Benzyl <i>p</i> -coumarate	—	—	4.13	4.60	5.28	5.36
Cinnamyl cinnamate	—	—	0.36	0.51	0.57	0.51
5-Methoxy pinobanksin	0.54	1.84	8.02	7.91	7.92	7.99
Pinobanksin	0.67	1.82	8.06	7.66	7.85	8.01
Quercetin	—	—	0.22	0.10	0.20	0.21
Alpinetin	—	0.09	1.13	1.15	1.08	1.04
Kaempferol	0.02	0.05	0.59	0.59	0.58	0.57
Apigenin	—	0.03	0.88	0.89	0.94	0.85
Isorhamnetin	—	0.23	3.59	3.63	2.90	3.03
Pinocembrin	0.11	1.39	37.42	40.39	38.25	38.69
Pinobanksin-3-O-acetate	—	2.35	66.93	69.36	67.67	69.12
Chrysin	—	0.39	20.03	23.90	25.33	23.66
Galangin	—	0.27	9.97	11.25	12.22	11.53
Pinostrobin	—	—	1.81	2.85	2.81	2.13
Tectochrysin	—	—	1.45	1.92	2.11	2.00

➤ In WEP, Identified 15 compounds, the main compounds were polar phenolic acids, such as caffeic acid, *p*-coumaric acid, isoferulic acid, and benzoic acid.

➤ In 75% EEP, Identified 28 compounds, contained polar phenolic acids and weak-polar phenolics, such as some flavonoids and phenolic acid esters

1 Background

Phenolics of Ethanol/Water Extracts

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Volume 2015, Article ID 595393, 9 pages
<http://dx.doi.org/10.1155/2015/595393>



Research Article

Effect of Ethanol/Water Solvents on Phenolic Profiles and Antioxidant Properties of Beijing Propolis Extracts

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Background

2

Inhibition on glucosidase

3

Inhibition on glycosylation

2 Inhibition on α -glucosidase



- ❖ In China, more than **92 million adults have diabetes**, and **95 percent of them are type 2 diabetes**.
- ❖ One important characteristic of diabetes is the increase in blood sugar levels after meals.
- ❖ Some **α -glucosidase inhibitors**, such as **acarbose**, have been approved for **clinical use** in the management of type 2 diabetes.

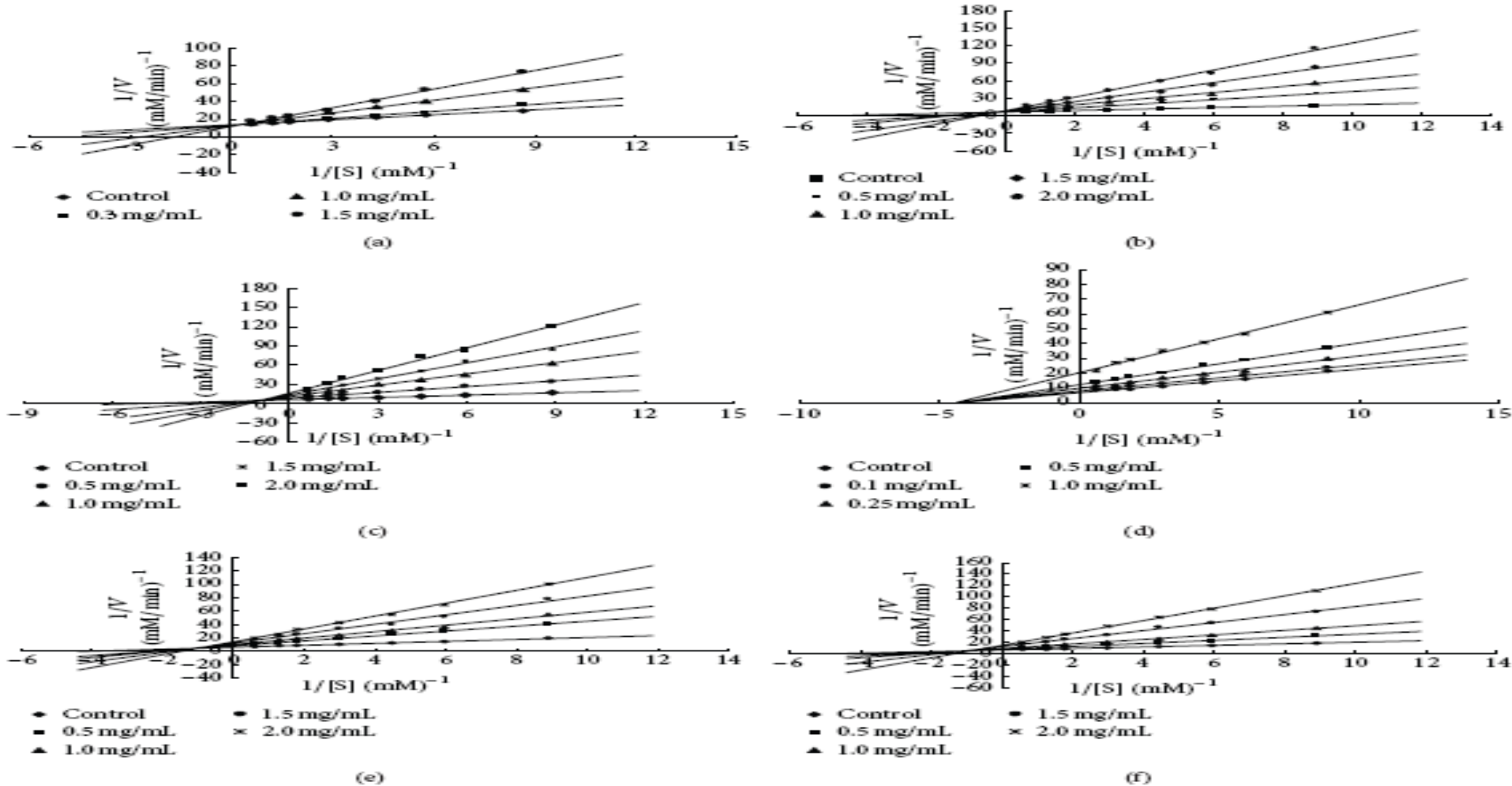
2 Inhibition on α -glucosidase

TABLE 2: Inhibition of propolis extracts against yeast and rat intestinal α -glucosidase.

Aqueous ethanol extracts of propolis (EEP)	Baker's yeast α -glucosidase	IC ₅₀ (μ g/mL)	
		Rat intestinal sucrase	Rat intestinal maltase
WEP	16.0 $\pm$ 1.38 ^{bc}	37.91 $\pm$ 0.52 ^{ab}	32.67 $\pm$ 0.24 ^e
25% EEP	11.32 $\pm$ 2.23 ^{ab}	40.25 $\pm$ 0.97 ^{ab}	44.80 $\pm$ 0.25 ^d
50% EEP	12.90 $\pm$ 1.14 ^b	53.12 $\pm$ 0.95 ^b	100.60 $\pm$ 2.95 ^b
75% EEP	7.24 $\pm$ 1.16 ^a	32.34 $\pm$ 0.61 ^a	71.82 $\pm$ 2.95 ^c
95% EEP	16.26 $\pm$ 0.43 ^{bc}	32.91 $\pm$ 0.54 ^a	102.76 $\pm$ 1.47 ^b
100% EEP	20.01 $\pm$ 1.54 ^c	38.06 $\pm$ 0.56 ^{ab}	131.12 $\pm$ 1.83 ^a
Acarbose	177.47 $\pm$ 6.28 ^d	538.30 $\pm$ 26.69 ^c	22.46 $\pm$ 0.86 ^f

- ❖ All aqueous ethanol extracts of propolis showed stronger inhibition against the α -glucosidase, compared to acarbose
- ❖ Especially, using the higher concentration of ethanol as the solvent, GOT THE BETTER RESULTS
- ❖ The 75% ethanol extracts of propolis (75% EEP) showed the highest inhibitory effect on α -glucosidase and sucrase

2 Inhibition on α -glucosidase



- The inhibition of WEP and 25% EEP was competitive inhibition mode
- 75% EEP was noncompetitive inhibition

2 Inhibition on α -glucosidase

TABLE 3: Inhibitory kinetics and K_i values of various propolis extracts against baker's yeast α -glucosidase.

Aqueous ethanol extracts of propolis (EEP)	Kinetic mode	K_i ($\mu\text{g/mL}$)
WEP	Competitive inhibition	10.43 ± 1.41^b
25% EEP	Competitive inhibition	9.85 ± 2.48^b
50% EEP	Mixed inhibition	9.92 ± 0.43^b
75% EEP	Noncompetitive inhibition	15.18 ± 0.58^a
95% EEP	Mixed inhibition	9.65 ± 1.54^b
100% EEP	Mixed inhibition	10.89 ± 2.84^b

- ❖ these propolis extracts as **noncompetitive or mixed inhibitors** show a broader specificity of inhibition
- ❖ the ability to bind to wider regions of enzyme other than the active site of competitive inhibitor

2 Inhibition on α -glucosidase

Evidence-Based Complementary and Alternative Medicine
Volume 2015, Article ID 587383, 7 pages
<http://dx.doi.org/10.1155/2015/587383>



Research Article

Inhibitory Properties of Aqueous Ethanol Extracts of Propolis on Alpha-Glucosidase

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Background

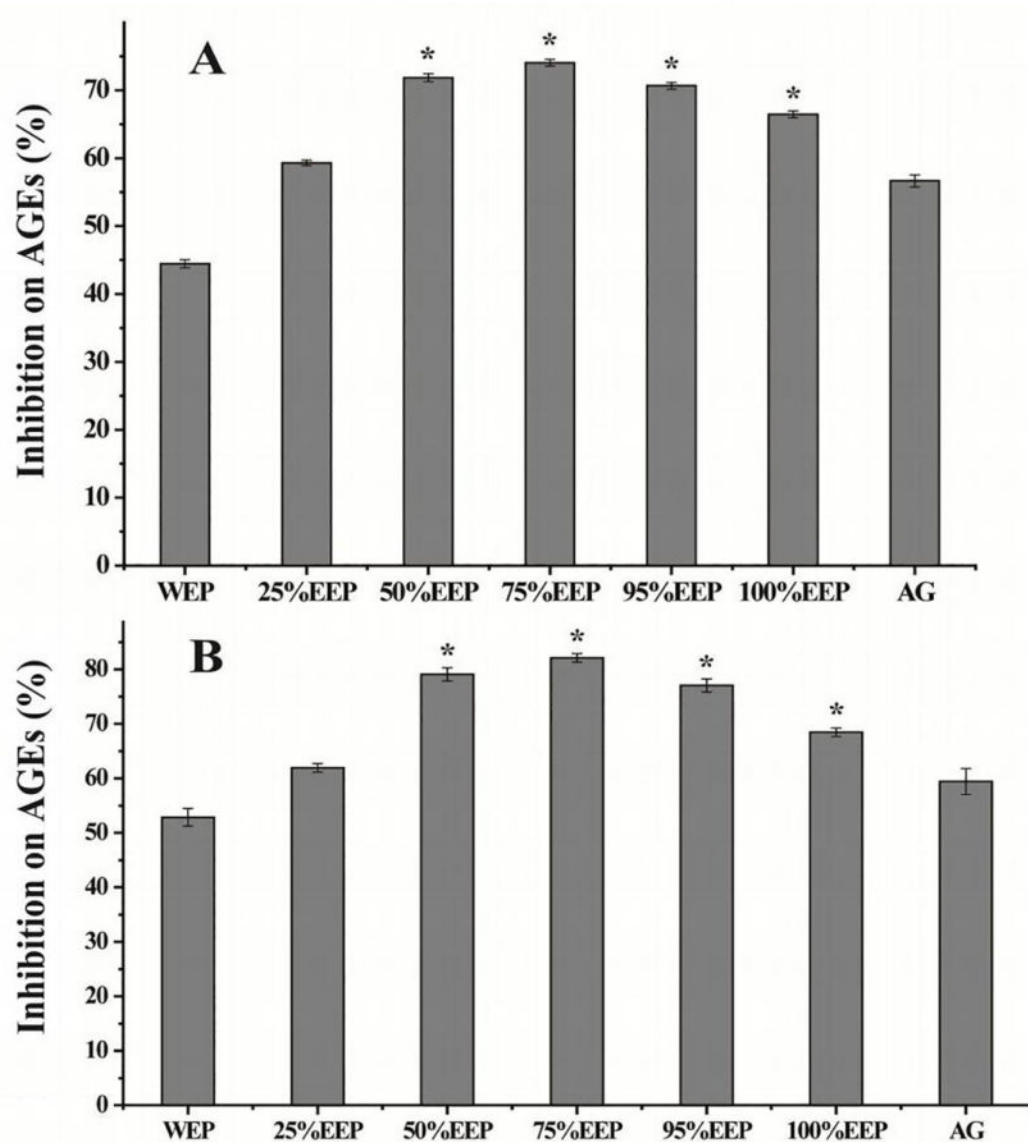
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Inhibition on glucosidase

3

Inhibition on glycosylation

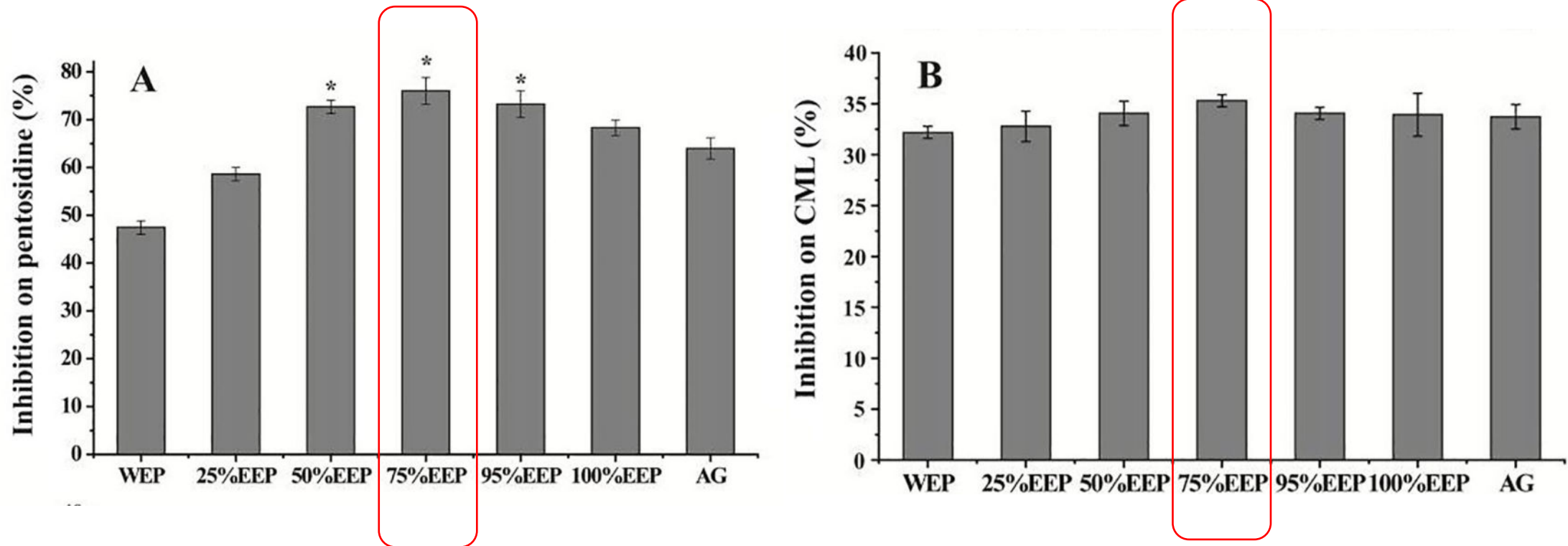
3 Inhibition on ended glycosylation products



- ❖ Diabetes complications include retinopathy, cataracts, atherosclerosis, neuropathy, nephropathy, and impaired wound healing due to AGEs accumulation;
- ❖ Notably, the inhibitory effects of 50%, 75%, 95%, and 100% EEP on total AGEs formation were significantly superior to those of the positive control AG (aminoguanidine);
- ❖ The 75% ethanol extract (75% EEP) exhibited the highest inhibitory effect on the glycation of BSA-glucose and BSA-MGO model.

3 Inhibition on ended glycosylation products

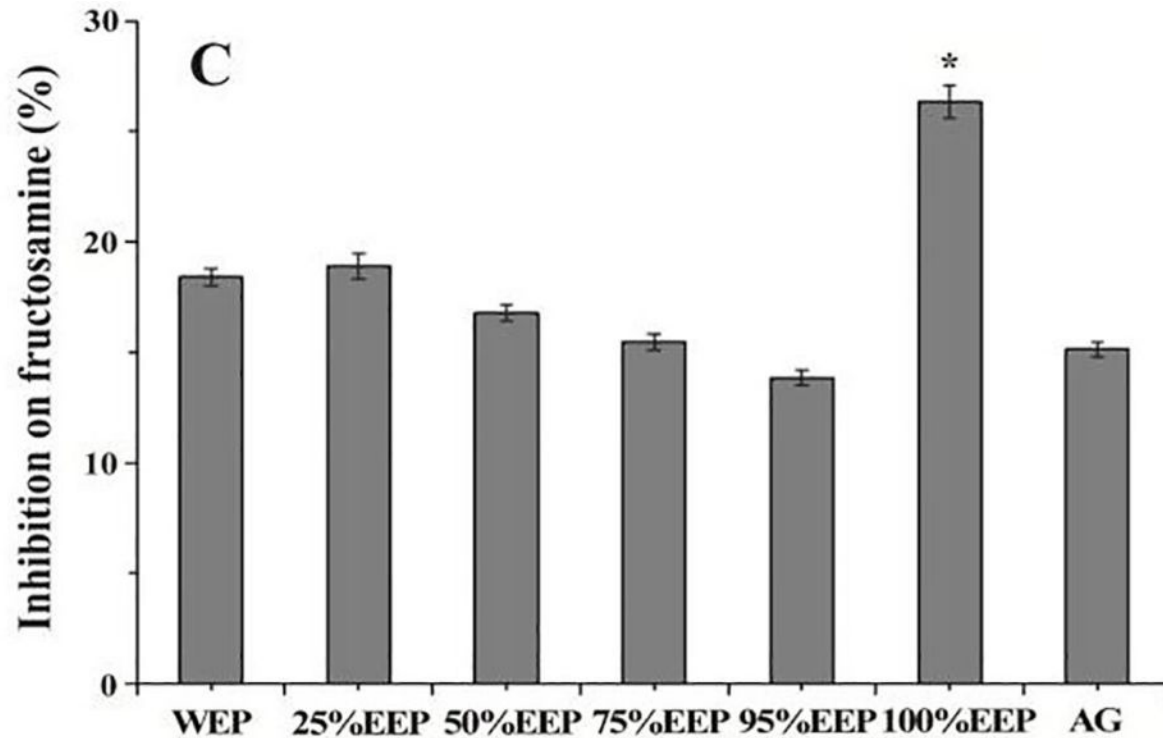
Propolis Extracts on Pentosidine (A) and CML (B)



- 75% EEP had the highest inhibitory rates for both pentosidine (76.02%) and CML (35.3%).

3 Inhibition on ended glycosylation products

Propolis Extracts on Fructosamine



- ❖ Inhibitory rates of propolis extracts were comparable to or slightly higher than 1 mM AG solution.
- ❖ The 100% ethanol extract (100% EEP) exhibited the highest inhibitory effect, and better than that of AG as positive control.

3 Inhibition on ended glycosylation products

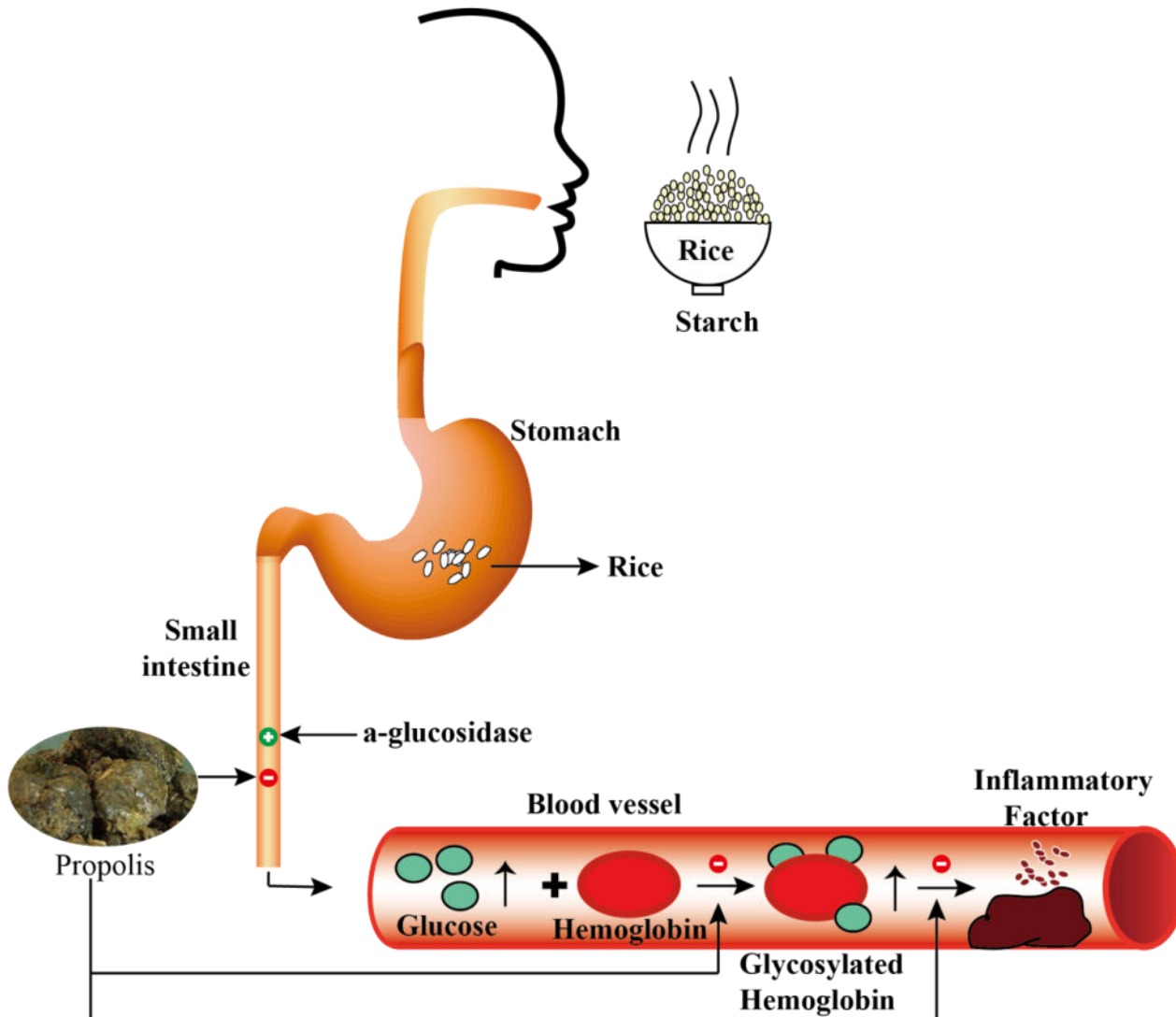


Article

Inhibitory Effects of Aqueous Ethanol Extracts of Poplar-Type Propolis on Advanced Glycation End Products and Protein Oxidation

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and Hongcheng Zhang ^{5,*} 

Summaries



- ❖ Chinese propolis belongs to **phenolic resins** and is only from poplar buds;
- ❖ **75 % ethanol/water solvent** may be the best for the higher extraction yield for poplar-type propolis;
- ❖ All aqueous ethanol extracts of propolis showed the stronger inhibition against the α -glucosidase;
- ❖ All aqueous ethanol extracts of propolis showed the stronger **inhibition on the formation of AGEs**

MANY THANKS FOR ATTENTION

