JUNI

Neuro-Psychiatrie

iCANN LIFE SCIENCES

Satellite Symposium

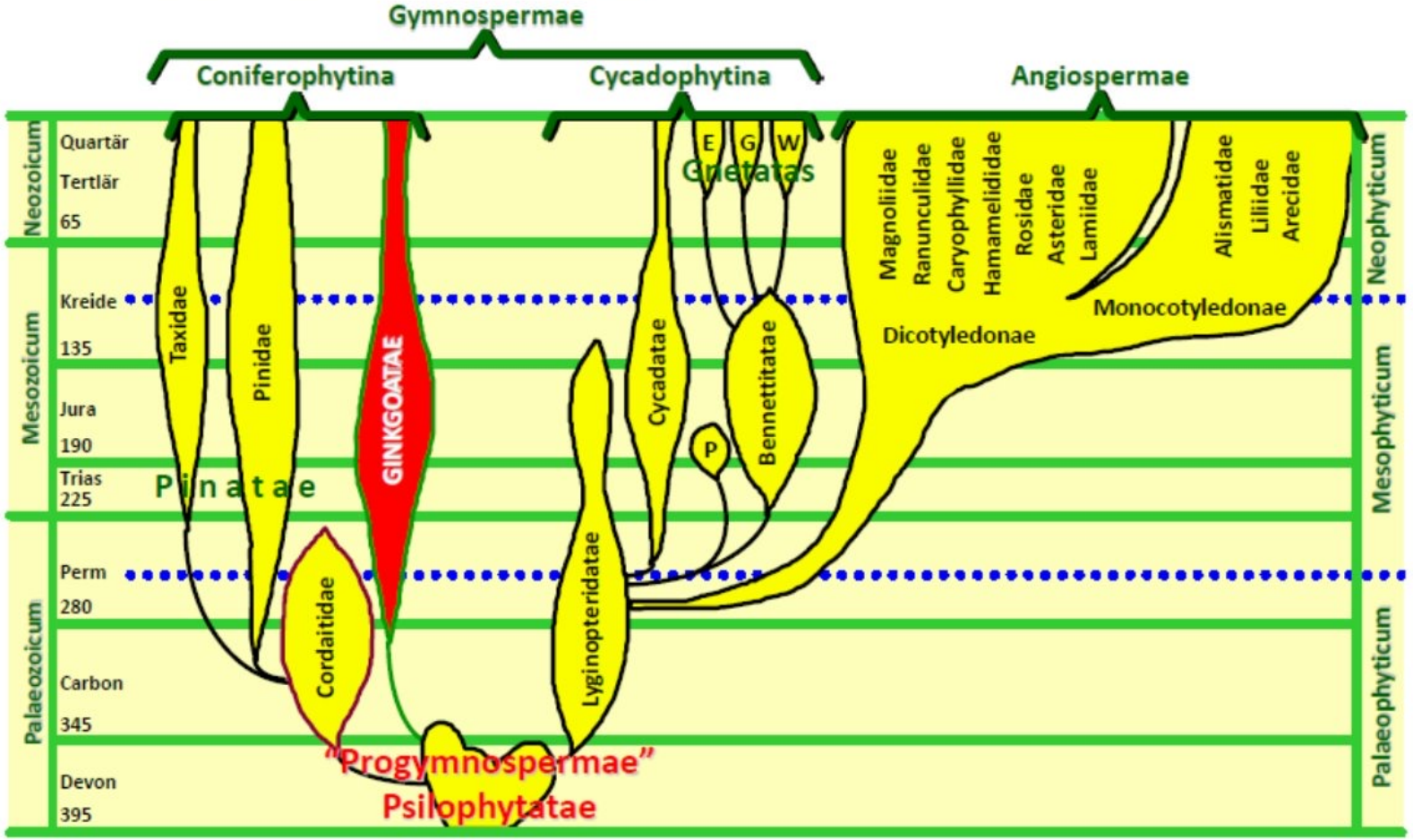
24 Juin 2023

WILLPHARMA
- SINCE 1924 -

Part I: 5 - 8 min

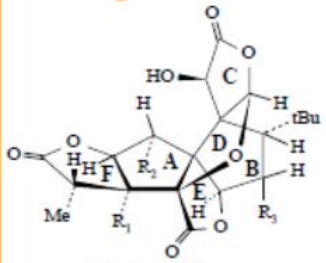
LE Ginkgo biloba et son action prolongée de 24h.

GINKGOATAE: AN UNMODIFIED PHYLUM THROUGH THE CENTURIES

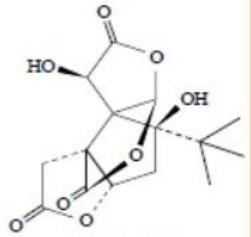


MAIN ACTIVES OF THE CLINICALLY TESTED STANDARDIZED EXTRACT

Main terpenic constituents of *Ginkgo biloba* standardized extract



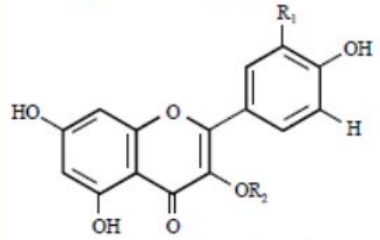
Ginkgolides



Bilobalide

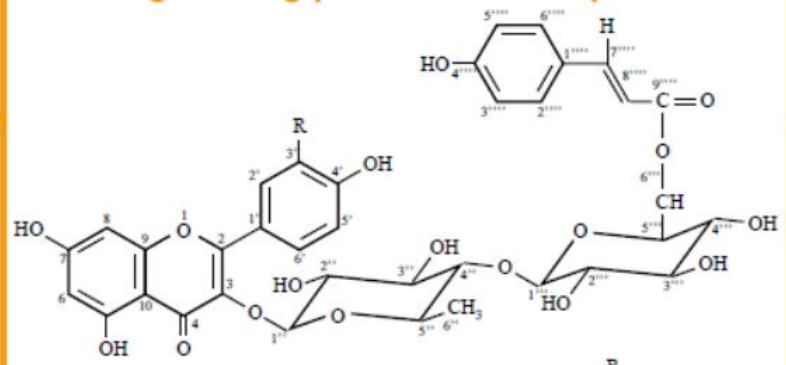
Ginkgolide	R_1	R_2	R_3
A	OH	H	H
B	OH	OH	H
C	OH	OH	OH
J	OH	H	OH
M	H	OH	OH

Ginkgoflavonglycosides



	R_1	R_2
1) Astragalin	H	Gl
2) Rutin	OH	Gl-Rh
3) Isorutin	OH	Rh-Gl
4) Kaempferol-3-O-Gl-Rh	H	Gl-Rh
5) Kaempferol-7-O-Gl	H	Gl
6) Isoquercitrin	OH	Gl
7) Isorhamnetin-3-O-Rh-Rh-Gl	OCH_3	Rh-Rh-Gl
8) Quercetrin-3-O-Rh-Rh-Gl	OH	Rh-Rh-Gl

Ginkgoflavonglycosides coumaroyl esters



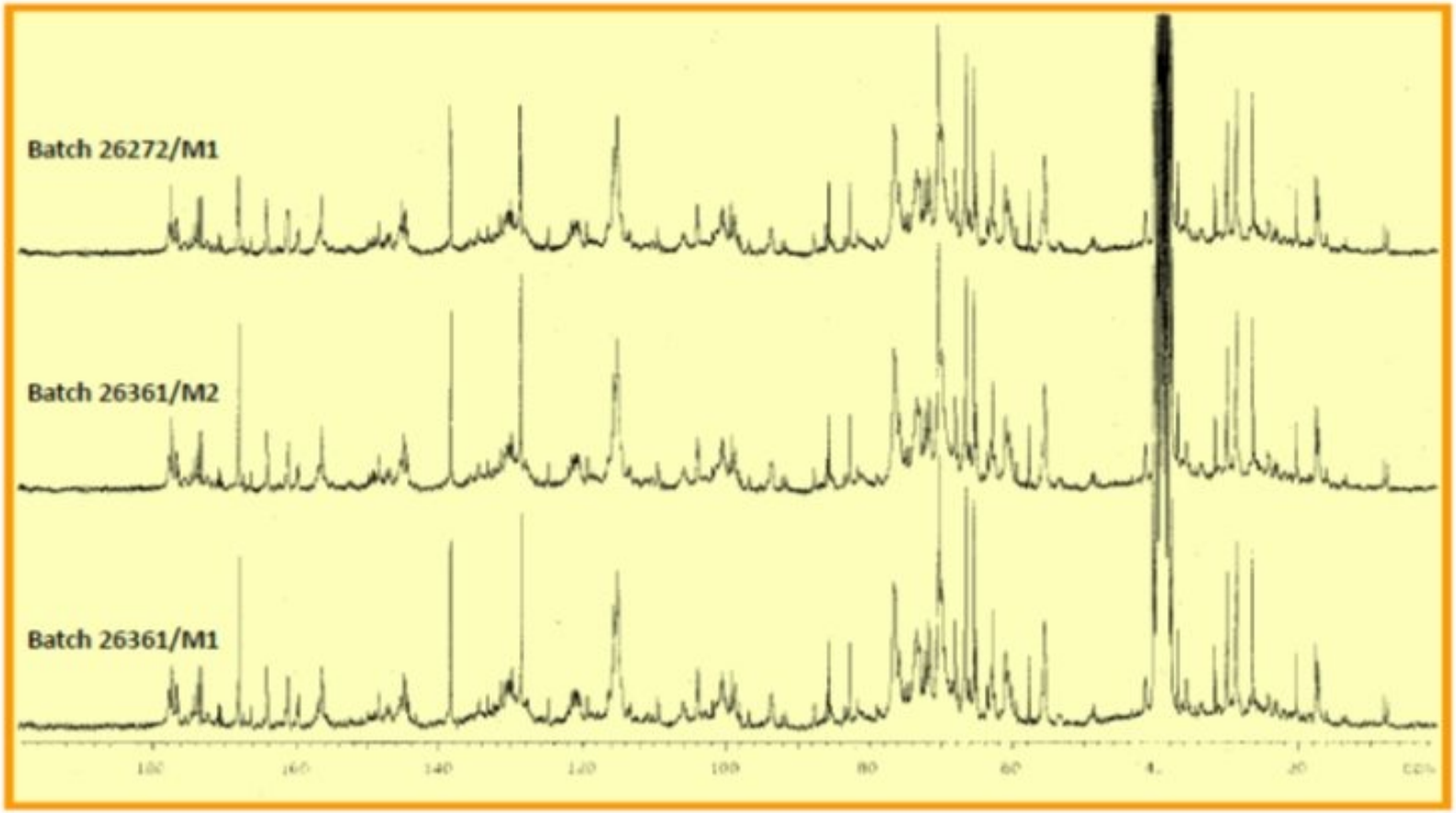
	R
9) Kaempferol-3-O-α-(6‴coumaroylglucosyl-β-1,4-rhamnoside)	H
10) Quercetin-3-O-α-(6‴coumaroylglucosyl-β-1,4-rhamnoside)	OH
11) Isorhamnetin-3-O-α-(6‴coumaroylglucosyl-β-1,4-rhamnoside)	OCH_3

indena

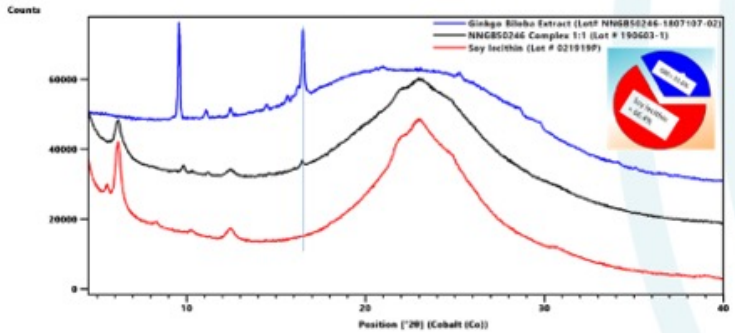
≥24% of ginkgoflavoglucosides by HPLC

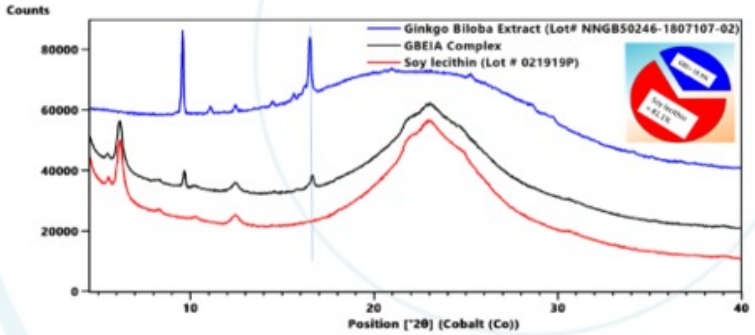
≥6% as sum of ginkgolides A, B,C and bilobalide by HPLC

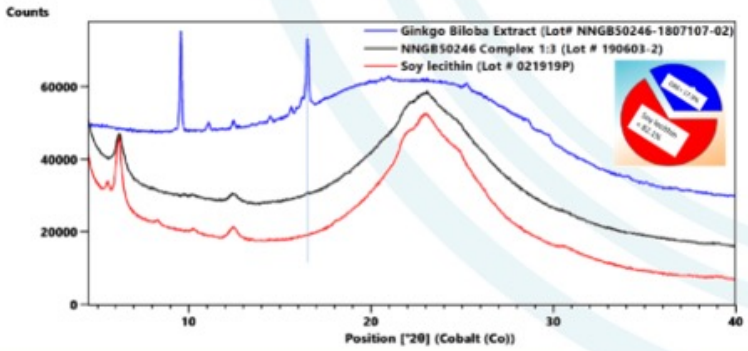
≤5 ppm of total ginkgolic acids by HPLC



Network Nutrition®
Part of IMCD







X-Ray Diffraction (XRD) scientifically validates a key design feature in Ginkgosome™.

Analytically verified superior liposomal formation and structural integrity.

IMCD

UNSW AUSTRALIA
Value through expertise

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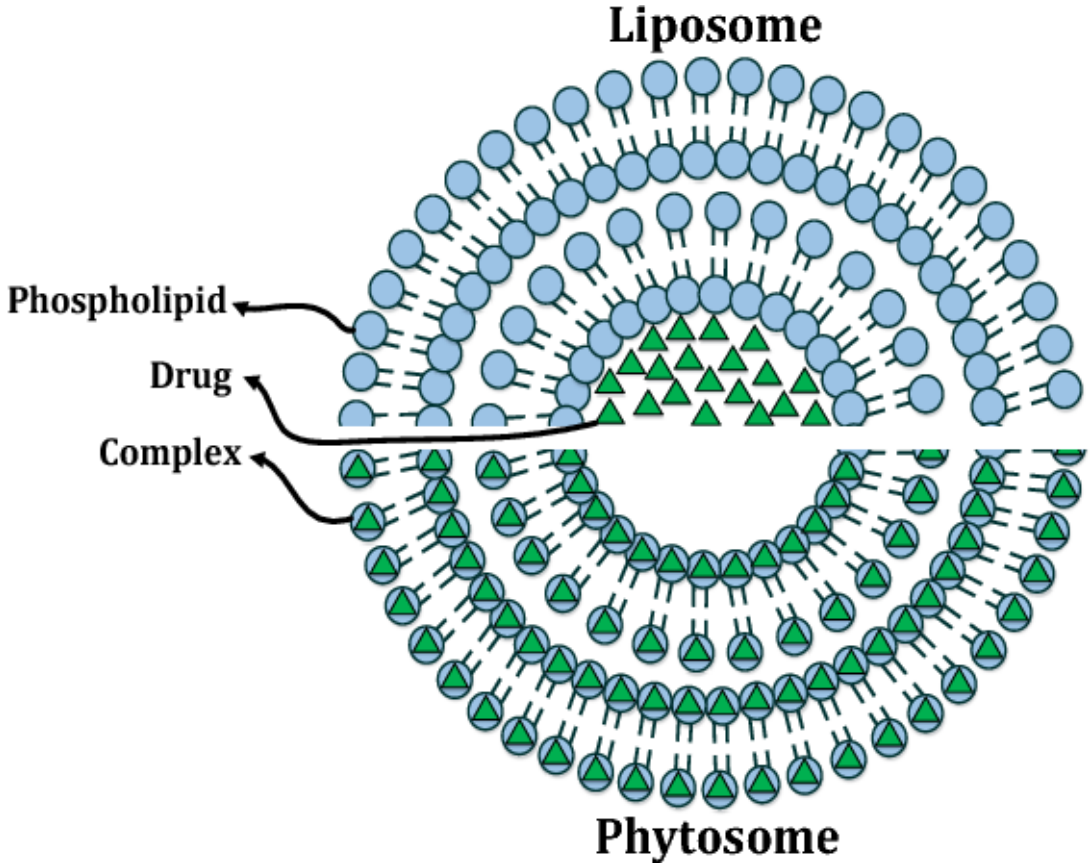
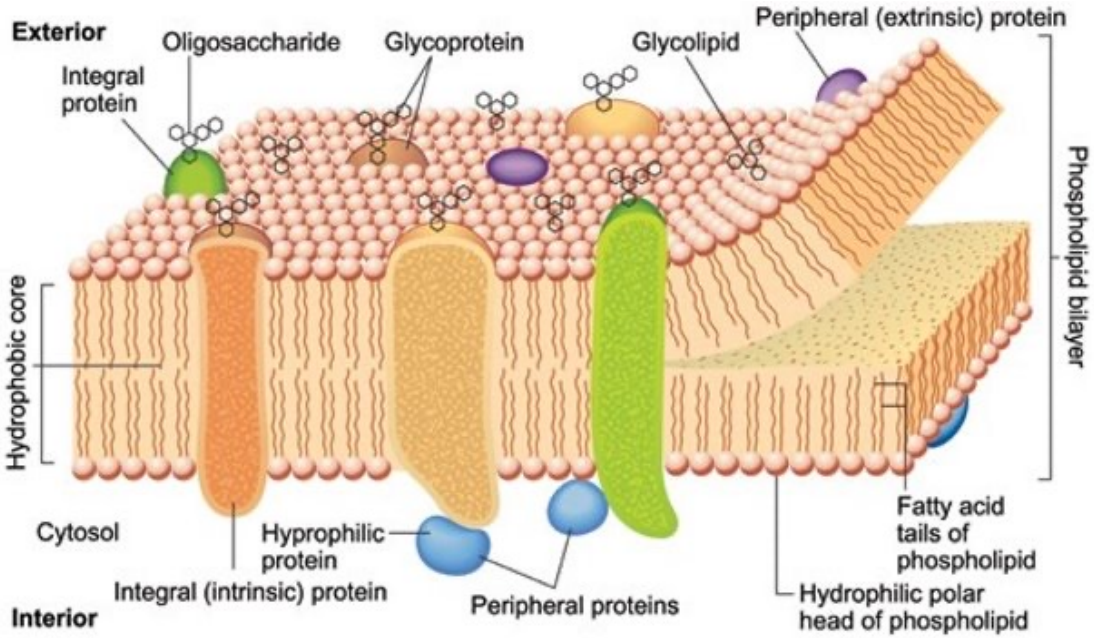
PS: Key element to create Ginkgosome





Kennedy et al. (p. 204)

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(www.interscience.wiley.com) **DOI**: 10.1002/hup.837

Acute cognitive effects of standardised Ginkgo biloba extract complexed with phosphatidylserine

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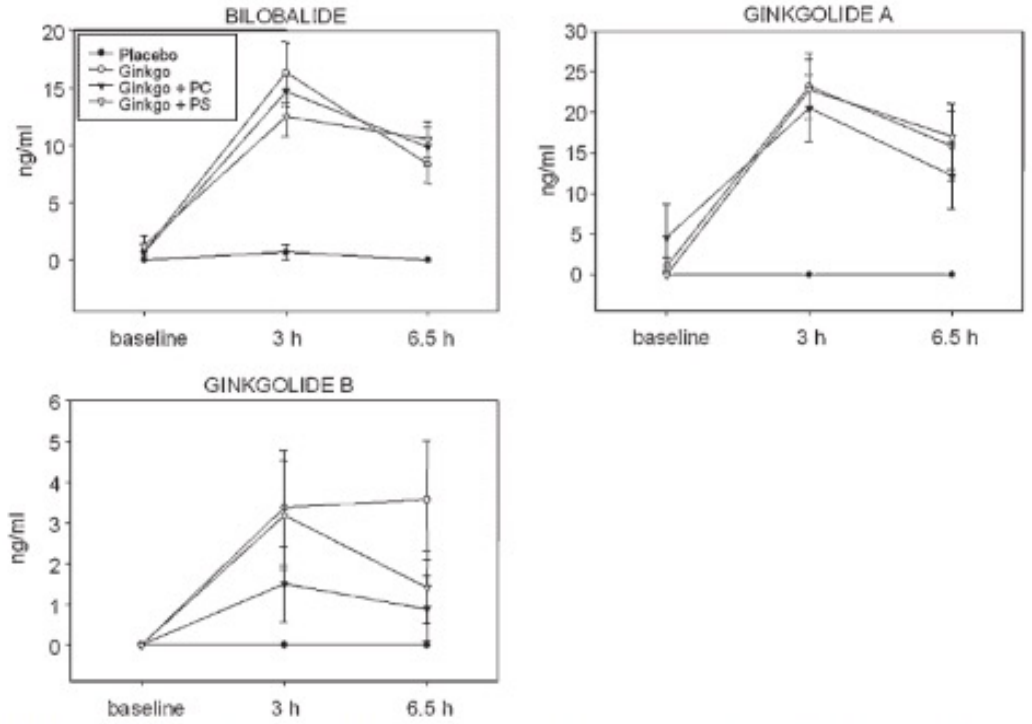

Figure 1. Mean levels of bilobalide and ginkgolids A and B in serum samples taken at baseline, 3 and 6.5 h post-dose. The figure represents data from the 13 participants that provided a full set of samples

Kennedy et al. (p. 205)

Measure		Pre-dose Baseline score	Change from baseline score 1 hr post-dose	2.5hr post-dose	4 hr post-dose	6hr post-dose
Immediate Word Recall (% accuracy)	placebo	51.90	-6.05	-5.71	-6.43	-9.76
	Ginkgo	51.43	-3.81	-6.31	-6.19	-8.33
	Gink+PC	47.74	-4.29	-2.26	-9.17	-5.12
	Gink+PS	47.86	-3.21	-6.71	-2.62	-7.26
Simple Reaction time (msecs)	placebo	287.34	9.60	2.21	2.36	-0.42
	Ginkgo	283.99	10.90	20.59	14.56	27.92
	Gink+PC	290.59	5.83	2.06	15.10	10.82
	Gink+PS	294.16	12.52	11.13	10.24	19.73
Digit Vigilance Accuracy (%)	placebo	95.48	-0.35	-0.58	-0.95	-2.14
	Ginkgo	95.87	-2.38	-3.17	-1.67	-3.25
	Gink+PC	94.76	0.68	-1.11	-0.63	-0.63
	Gink+PS	97.46	1.91	-0.75	1.75	-0.87
Digit Vigilance False alarms (number)	placebo	0.93	0.04	0.68	0.29	0.43
	Ginkgo	1.07	0.18	-0.29	-0.04	0.68
	Gink+PC	0.86	-0.04	0.18	0.36	0.00
	Gink+PS	1.21	-0.04	-0.18	-0.21	0.71
Digit Vigilance Reaction time (msecs)	placebo	434.45	9.34	23.77	15.55	25.78
	Ginkgo	435.88	14.43	6.84	15.67	14.38
	Gink+PC	436.13	16.46	17.97	22.86	16.57
	Gink+PS	453.16	5.63	8.25	4.94	8.44
Choice reaction time accuracy (%)	placebo	93.43	0.36	0.64	0.64	0.00
	Ginkgo	94.86	-0.36	-1.14	-1.29	-1.86
	Gink+PC	95.14	0.21	-0.64	-1.43	-1.14
	Gink+PS	94.71	-0.25	-0.57	-1.86	-1.75
Choice reactionTime (msecs)	placebo	419.05	-3.87	5.70	-2.50	-2.69
	Ginkgo	413.55	12.43	-1.57	4.22	7.82
	Gink+PC	419.04	1.36	-4.53	-1.89	4.02
	Gink+PS	422.03	-3.22	-13.9	-11	-3.05
Spatial Memory (%>chance)	placebo	93.13	-10.3	-11.6	-9.46	-6.73
	Ginkgo	90.18	-6.74	-6.83	-5.54	-2.81
	Gink+PC	90.54	-0.89	-5.85	-13.7	-8.84
	Gink+PS	89.33	-4.60	-2.77	-5.67	-3.26
Spatial memory Reaction time (msecs)	placebo	500.93	-17.3	-3.50	1.77	-36.6
	Ginkgo	487.69	-9.87	9.81	19.36	1.50
	Gink+PC	488.98	2.35	-6.89	13.03	-15.8
	Gink+PS	526.95	-25.8	-30.5	-20.9	-69.5
Numeric Working Memory (%>chance)	placebo	89.05	-3.41	-5.16	-5.72	-4.75
	Ginkgo	87.86	-2.22	-2.14	-3.09	-5.48
	Gink+PC	89.13	-4.92	-3.73	-3.81	-5.16
	Gink+PS	85.56	-1.03	-2.46	-3.33	-3.18
Numeric Work'g Memory RT (msecs)	placebo	519.67	-9.12	-17.5	-7.55	-2.41
	Ginkgo	509.01	7.42	-7.45	1.60	6.65
	Gink+PC	513.66	6.71	-9.14	13.78	0.98
	Gink+PS	540.21	-24.7	-28.5	-48.2	-31.6
Delayed Word Recall (% accuracy)	placebo	38.69	-5.48	-12	-12	-16.7
	Ginkgo	37.14	-6.19	-11.6	-9.64	-13.8
	Gink+PC	35.60	-7.62	-7.14	-13.1	-9.64
	Gink+PS	33.93	-7.02	-11.3	-8.93	-12
Word Recognition (%>chance)	placebo	65.00	-13.8	-12.9	-14.5	-16.7
	Ginkgo	65.90	-6.43	-7.86	-7.14	-12.1
	Gink+PC	65.24	-8.34	-7.38	-9.05	-11.7
	Gink+PS	65.48	-13.1	-11.2	-12.4	-16.2
Word Recognition Reaction time (msecs)	placebo	662.54	-5.78	-6.62	13.68	-6.92
	Ginkgo	642.37	17.86	11.83	15.74	19.28
	Gink+PC	646.92	21.82	16.54	25.16	-0.39
	Gink+PS	710.53	-55.2	-68.2	-48.2	-48.6
Picture Recognition (%>chance)	placebo	60.60	-13.9	-14.1	-9.82	-13.7
	Ginkgo	60.18	-11	-12.5	-8.57	-11
	Gink+PC	61.25	-11.6	-7.32	-7.86	-15.4
	Gink+PS	61.96	-2.86	-3.75	1.43	-0.64
Picture recognition Reaction time (msecs)	placebo	755.86	15.11	-11.0	-33.7	-2.29
	Ginkgo	755.94	11.23	-31.4	19.67	-32.4
	Gink+PC	747.12	24.96	-10.8	56.22	29.96
	Gink+PS	796.49	-26.4	-54	-45.2	-76.2

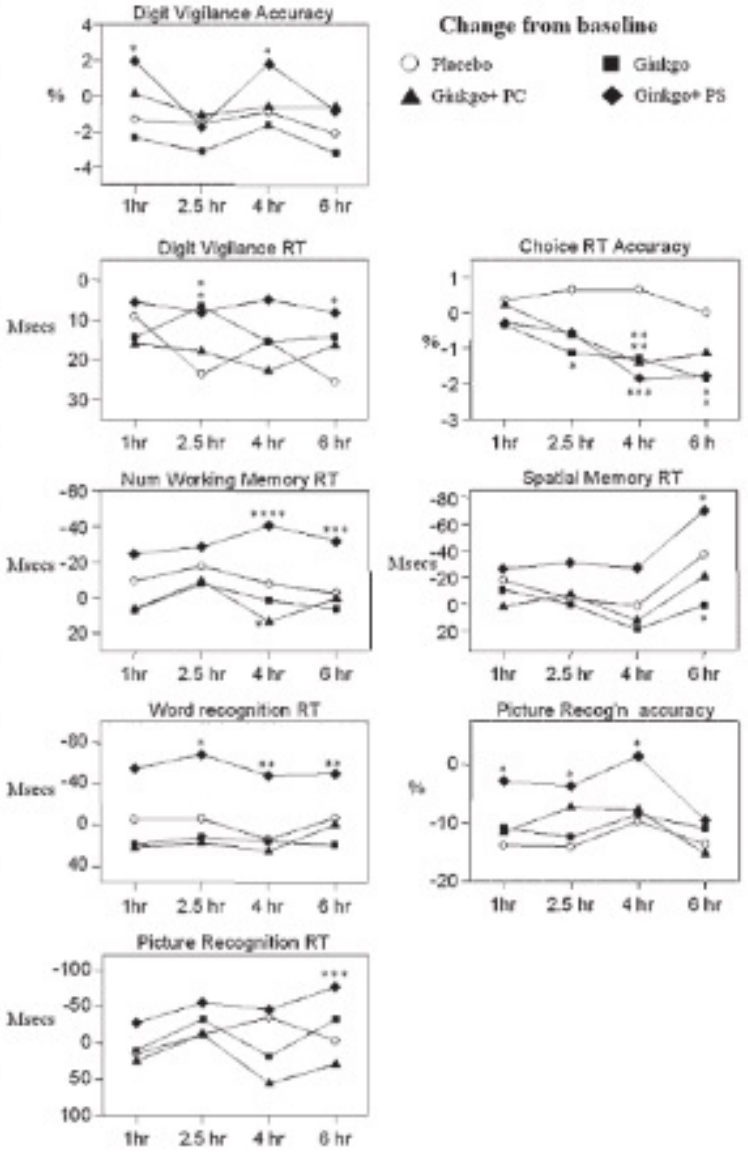

Figure 2. Effects of the treatments on the individual task outcome measures from the CDR battery. Mean baseline and change from baseline scores (with standard errors) are presented. Tasks are displayed in order of completion, with a graphical representation of measures generating significant differences on the initial ANOVA and subsequent planned comparisons (*, $p < 0.05$; **, $p < 0.01$; ***, $p < 0.005$; ****, $p < 0.001$ compared to placebo). Ginkgo + PC = Ginkgo complexed with phosphatidylserine; Ginkgo + PS = Ginkgo complexed with phosphatidylserine

Factor		Pre-dose Baseline score	Change from baseline score: 1 hr post-dose	2.5hr post-dose	4 hr post-dose	6hr post-dose
Speed of Attention	placebo	1150.8	14.96	31.68	15.41	22.67
	Ginkgo	1133.4	37.75	25.86	34.45	50.12
	Gink+PC	1145.8	23.26	15.50	36.07	31.40
	Gink+PS	1179.3	14.93	5.45	4.16	24.32
Accuracy of Attention	placebo	88.75	-0.46	-1.07	-0.39	-1.39
	Ginkgo	89.50	-1.43	-1.71	-1.36	-3.07
	Gink+PC	89.36	0.18	-1.00	-1.36	-0.86
	Gink+PS	87.75	0.75	-0.89	0.07	-2.00
Speed of Memory	placebo	2438.2	-17.08	-38.66	-25.80	-48.19
	Ginkgo	2395.0	26.63	-27.05	56.38	-5.00
	Gink+PC	2396.1	55.85	-10.10	108.19	10.64
	Gink+PS	2574.2	-132.2	-181.3	-160.5	-227.3
Quality of Memory	placebo	397.77	-50.99	-62.47	-57.98	-66.34
	Ginkgo	382.74	-37.36	-47.19	-40.18	-54.54
	Gink+PC	379.49	-37.66	-33.69	-56.68	-55.78
	Gink+PS	364.11	-31.82	-37.19	-31.50	-52.50
Secondary Memory	placebo	215.69	-37.26	-45.65	-42.80	-56.85
	Ginkgo	204.70	-28.39	-38.21	-31.55	-46.25
	Gink+PC	199.82	-31.85	-24.11	-39.17	-41.79
	Gink+PS	189.23	-26.19	-31.96	-22.50	-46.07
Working Memory	placebo	182.16	-13.73	-16.81	-15.18	-9.50
	Ginkgo	178.04	-8.96	-8.97	-8.63	-8.29
	Gink+PC	179.66	-5.81	-9.58	-17.51	-14.00
	Gink+PS	174.89	-5.63	-5.23	-9.00	-6.43

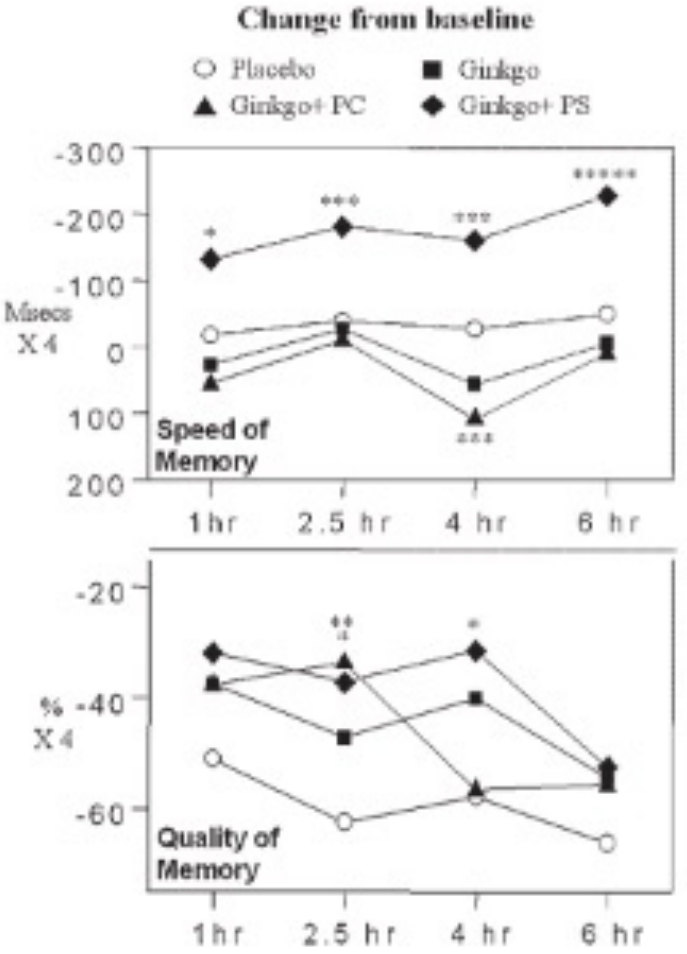

Figure 3. Effects of the treatments on the primary outcome cognitive factors derived from the CDR battery outcomes. Mean baseline and change from baseline scores (with standard errors) are presented, with a graphical representation of the factors generating significant differences on the initial ANOVA and subsequent planned comparisons (*, $p < 0.05$; **, $p < 0.01$; ***, $p < 0.005$; *****, $p < 0.0005$ compared to placebo). Ginkgo + PC = Ginkgo complexed with phosphatidylserine; Ginkgo + PS = Ginkgo complexed with phosphatidylserine

Kennedy et al. (p. 206)

Briskey and Rao

Briskey and Rao
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https://doi.org/10.1186/s12906-022-03679-x

BMC Complementary Medicine and Therapies

RESEARCH Open Access

A double-blind, randomised cross-over study to evaluate the absorption of a commercially available *Ginkgo biloba* extract compared to the liposomal extract Ginkgosome

David Briskey[1,2] and Amanda Rao[1*]

Abstract

Background: *Ginkgo biloba* extracts (GBE) have been used in traditional medicines for centuries. GBE has been shown to deliver protective effects against symptoms of age-related cognitive decline. Despite there being standardised extractions for GBE, there is still variability in the absorption and efficacy of different extracts. Following the development of a liposomal GBE (Ginkgosome™), the aim of this study is to investigate the absorption of the liposomal formulation compared to a comparator formulation of equal dose.

Methods: Thirteen healthy male and female volunteers completed this single equivalent dose, randomised, double-blind crossover study. Plasma concentrations were determined at baseline and at regular intervals over a 24-h period following ingestion of 120 mg of either a liposomal or comparator formulation.

Results: The liposomal formulation was able to increase plasma concentration of ginkgolide B and C by 1.9 and 2.2-fold compared to the comparator formulation.

Conclusion: The novel liposomal formulation is safe in humans and demonstrates superior absorption for the supply of GBE constituents compared to a comparator standardised formulation.

Keywords: *Ginkgo biloba*, Absorption, Ginkgosome, Pharmacokinetics

Briskey and Rao

Table 2 GBE plasma absorption concentration, maximum plasma concentration and time to maximum concentration for GB, GC and BB for both groups. Data presented is the groups average based on the individual participants specific AUC, C_{max} and T_{max} data

	GB		GC		BB	
	Ginkgosome™	Standard	Ginkgosome™	Standard	Ginkgosome™	Standard
AUC	99.6 ± 52.8*	52.7 ± 17.7	4.2 ± 2.5*	1.9 ± 1.4	91.4 ± 38.8	86.6 ± 33.0
C_{max} (ng/mL)	13.2 ± 6.2*	7.8 ± 2.1	0.6 ± 0.1	0.5 ± 0.1	17.2 ± 7.1	19.6 ± 7.9
T_{max} (hrs)	4.6 ± 1.3*	2.5 ± 1.1	5.1 ± 1.2*	2.6 ± 1.6	4.5 ± 1.8*	1.8 ± 1.1

Values presented are values are mean ± SD

GB ginkgolide B, *GC* ginkgolide C, *BB* bilobalide, *AUC* area under the curve, C_{max} maximum concentration, T_{max} time for maximum concentration

* $p < 0.05$

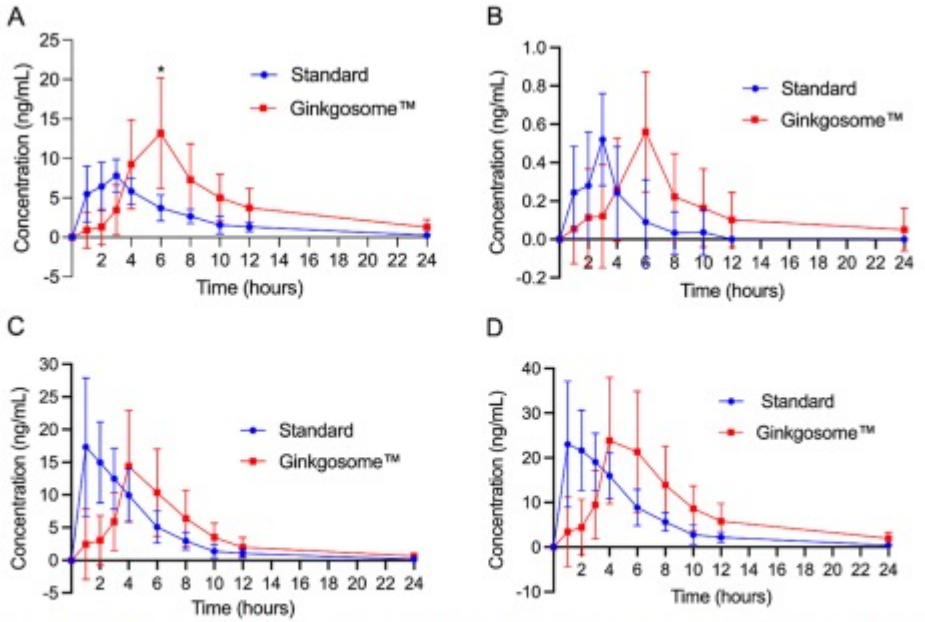

Fig. 1 **A** Plasma absorption of GB. **B** Plasma absorption of GC. **C** Plasma absorption of BB. D) Total (GB, GC & BB) plasma absorption over 24 h. * Significantly different C_{max} $p < 0.05$. Data presented is the groups average for each specific time point and may not represent the true C_{max} and/or T_{max} as presented in Table 2

Part II : 12-15 min

L'Huperzia serrata (qui contient de l'Huperzine A), l'inhibiteur naturel de l'acétylcholinestérase ?

40 mg Huperzia Serrata Extract = 400 µg Huperzine A

Friedli and Nibaldo C. Inestrosa

molecules

MDPI

Review

Huperzine A and Its Neuroprotective Molecular Signaling in Alzheimer's Disease

María Jesús Friedli [1] and Nibaldo C. Inestrosa [1,2,*]

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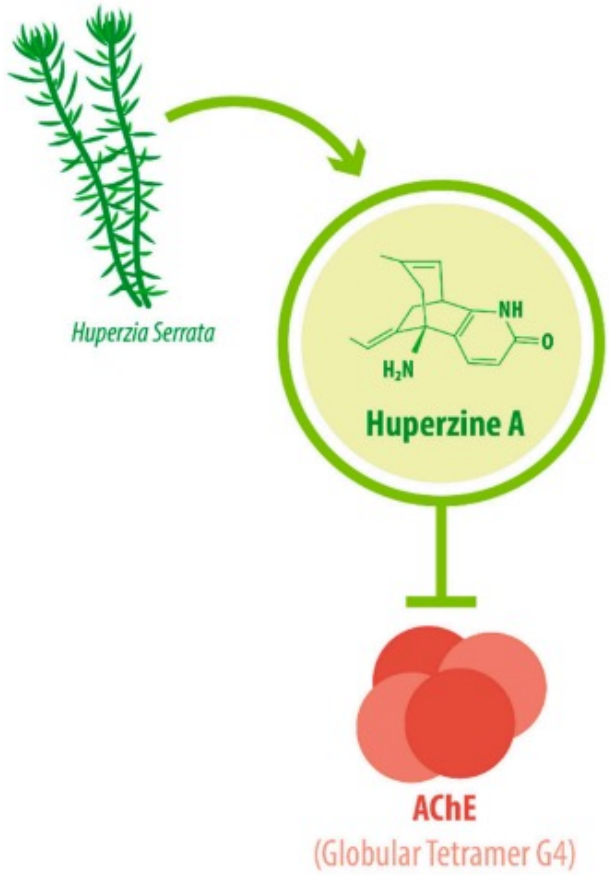
* Correspondence: ninestrosa@bio.puc.cl

Abstract: Huperzine A (HupA), an alkaloid found in the club moss *Huperzia serrata*, has been used for centuries in Chinese folk medicine to treat dementia. The effects of this alkaloid have been attributed to its ability to inhibit the cholinergic enzyme acetylcholinesterase (AChE), acting as an acetylcholinesterase inhibitor (AChEI). The biological functions of HupA have been studied both in vitro and in vivo, and its role in neuroprotection appears to be a good therapeutic candidate for Alzheimer´s disease (AD). Here, we summarize the neuroprotective effects of HupA on AD, with an emphasis on its interactions with different molecular signaling avenues, such as the Wnt signaling, the pre- and post-synaptic region mechanisms (synaptotagmin, neuroligins), the amyloid precursor protein (APP) processing, the amyloid-β peptide (Aβ) accumulation, and mitochondrial protection. Our goal is to provide an integrated overview of the molecular mechanisms through which HupA affects AD.

Friedli and Nibaldo C. Inestrosa

Mode d'action:

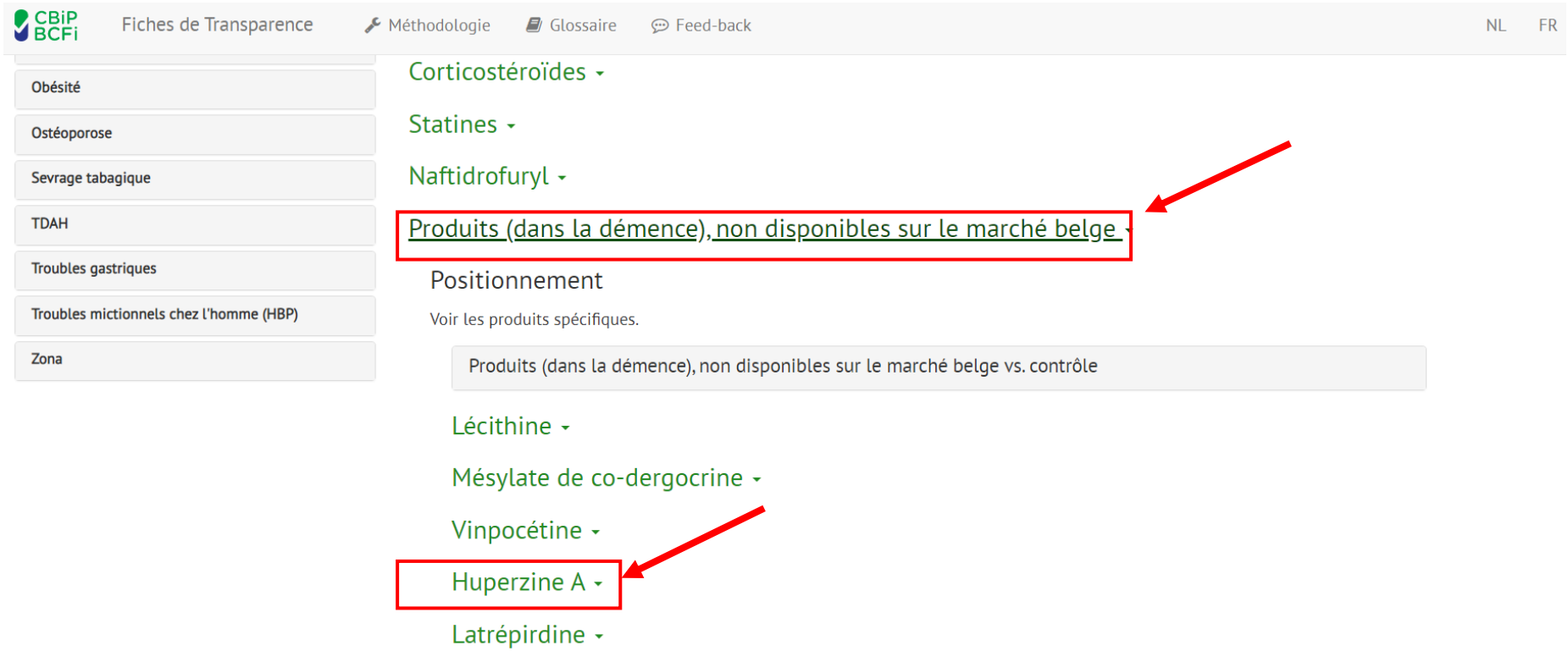


Friedli and Nibaldo C. Inestrosa

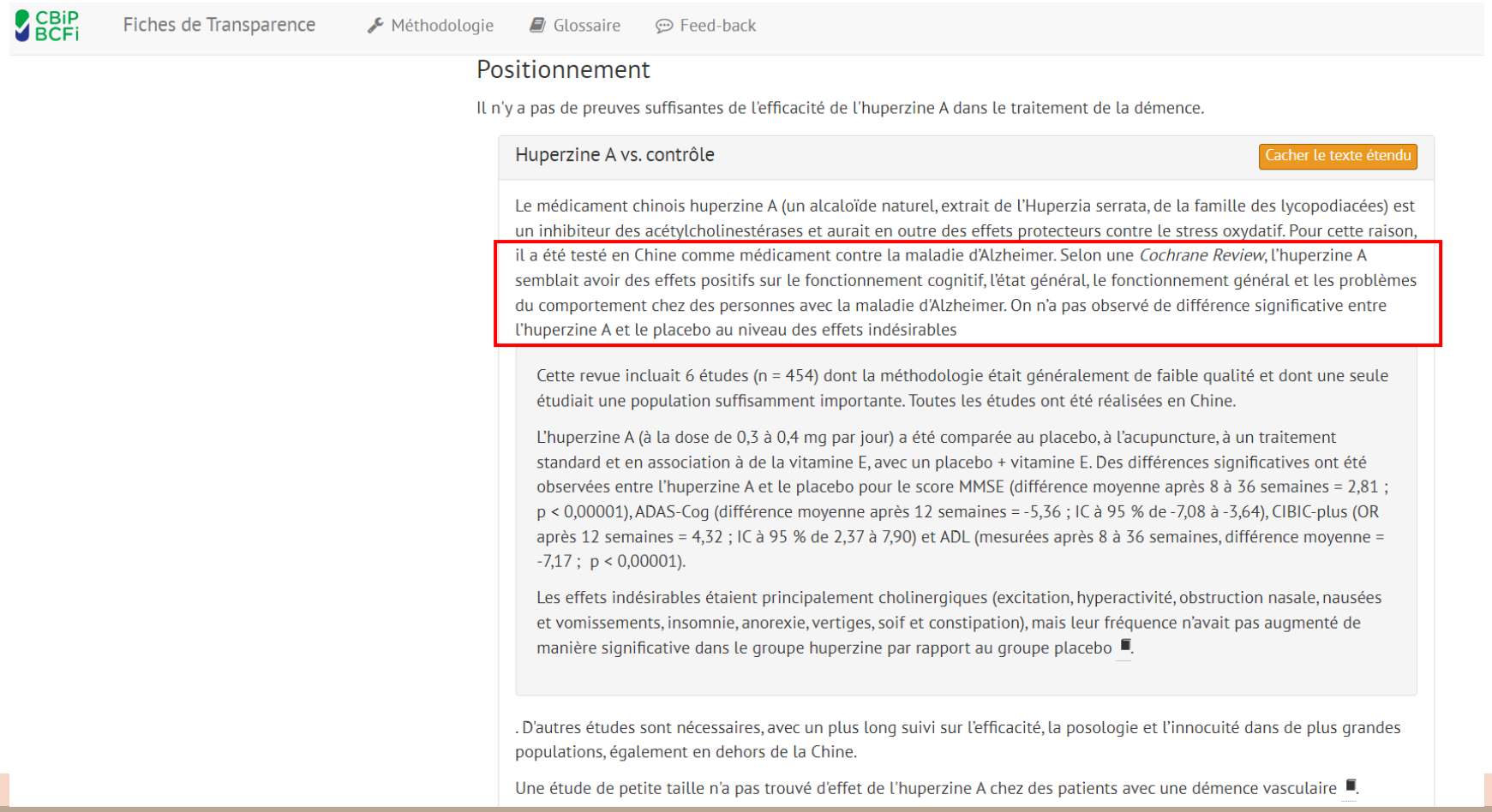
Table 1. Molecular targets of HupA's cholinergic mechanisms in dementia-related pathologies and effects of treatment.

Molecular Target	Effects of HupA Treatment	References
Inhibition of AChE	Reduced neuronal loss Decreased Aβ neurotoxicity]. Attenuated p53-mediated cell death Downregulated NF-kβ signaling Downregulated p65 translocation-related neurodegeneration [	[9,37,39,46,49]
Activation of α7-nAChRs and α4β2-nAChRs	Decreased NF-κB signaling Increased GABAergic transmission Reduced pro-inflammatory cytokines	[31,46,47]
Upregulation of Neurotrophin	Reduced loss of cholinergic neurons	[52]
Activation of BDNF/TrkB	Improved neuronal survival through PI3K/TrkB/mTOR signaling Induced LTP and synaptic transmission	[48,51,52,54]
Upregulation of Bcl-2 and downregulation of Bax	Decreased apoptotic activity	[38]
Upregulation of Synaptotagmin	Improved synaptic vesicle exocytosis	[48]
Interaction with ChE-like domain of Neuroligin-1	Decreased Aβ aggregation	[37,46,60]
Downregulation of activity of GSK-3β	Decreased tau phosphorylation and Aβ accumulation Increased neurogenesis and modulation of synaptic plasticity Increased nonamyloidogenic processing of APP] Downregulated NF-kβ signaling downregulated p65 expression-related neurodegeneration	[39,46,48,54]

CBIP – Huperzine A



CBIP – Huperzine A



CBiP BCFi Fiches de Transparence Méthodologie Glossaire Feed-back

Positionnement

Il n'y a pas de preuves suffisantes de l'efficacité de l'huperzine A dans le traitement de la démence.

Huperzine A vs. contrôle

Cacher le texte étendu

Le médicament chinois huperzine A (un alcaloïde naturel, extrait de l'Huperzia serrata, de la famille des lycopodiacées) est un inhibiteur des acétylcholinestérases et aurait en outre des effets protecteurs contre le stress oxydatif. Pour cette raison, il a été testé en Chine comme médicament contre la maladie d'Alzheimer. Selon une *Cochrane Review*, l'huperzine A semblait avoir des effets positifs sur le fonctionnement cognitif, l'état général, le fonctionnement général et les problèmes du comportement chez des personnes avec la maladie d'Alzheimer. On n'a pas observé de différence significative entre l'huperzine A et le placebo au niveau des effets indésirables

Cette revue incluait 6 études (n = 454) dont la méthodologie était généralement de faible qualité et dont une seule étudiait une population suffisamment importante. Toutes les études ont été réalisées en Chine.

L'huperzine A (à la dose de 0,3 à 0,4 mg par jour) a été comparée au placebo, à l'acupuncture, à un traitement standard et en association à de la vitamine E, avec un placebo + vitamine E. Des différences significatives ont été observées entre l'huperzine A et le placebo pour le score MMSE (différence moyenne après 8 à 36 semaines = 2,81 ; p < 0,00001), ADAS-Cog (différence moyenne après 12 semaines = -5,36 ; IC à 95 % de -7,08 à -3,64), CIBIC-plus (OR après 12 semaines = 4,32 ; IC à 95 % de 2,37 à 7,90) et ADL (mesurées après 8 à 36 semaines, différence moyenne = -7,17 ; p < 0,00001).

Les effets indésirables étaient principalement cholinergiques (excitation, hyperactivité, obstruction nasale, nausées et vomissements, insomnie, anorexie, vertiges, soif et constipation), mais leur fréquence n'avait pas augmenté de manière significative dans le groupe huperzine par rapport au groupe placebo .

. D'autres études sont nécessaires, avec un plus long suivi sur l'efficacité, la posologie et l'innocuité dans de plus grandes populations, également en dehors de la Chine.

Une étude de petite taille n'a pas trouvé d'effet de l'huperzine A chez des patients avec une démence vasculaire .

Cochrane Review

Cochrane Library

Cochrane Database of Systematic Reviews

Huperzine A for Alzheimer's disease (Review)

Li J, Wu HM, Zhou RL, Liu GJ, Dong BR

Cochrane Library

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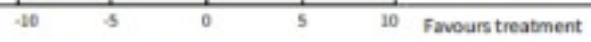
Cochrane Database of Systematic Reviews

Analysis 1.1. Comparison 1 Huperzine A versus placebo only, Outcome 1 The change of general cognitive function measured by MMSE.

Study or subgroup	Treatment N	Treatment Mean(SD)	Control N	Control Mean(SD)	Mean Difference Fixed, 95% CI	Weight	Mean Difference Fixed, 95% CI
Liu 1995	14	0.4 (10.2)	14	2 (7.2)		2.1%	-1.6[-8.14,4.94]
Xu 1997	50	3 (7.9)	53	0.4 (8)		9.48%	2.55[-0.52,5.62]
Yang 2003	35	4.3 (3.1)	30	0.1 (3.3)		37.32%	4.2[2.65,5.75]
Zhou 2004b	12	1.6 (2.1)	12	-0.4 (1)		51.11%	2.03[0.71,3.35]
Total ***	**111**		**109**			**100%**	**2.81[1.87,3.76]**

Heterogeneity: Tau^2=0; Chi^2=6.2, df=3(P=0.1); I^2=51.65%

Test for overall effect: Z=5.83(P<0.0001)



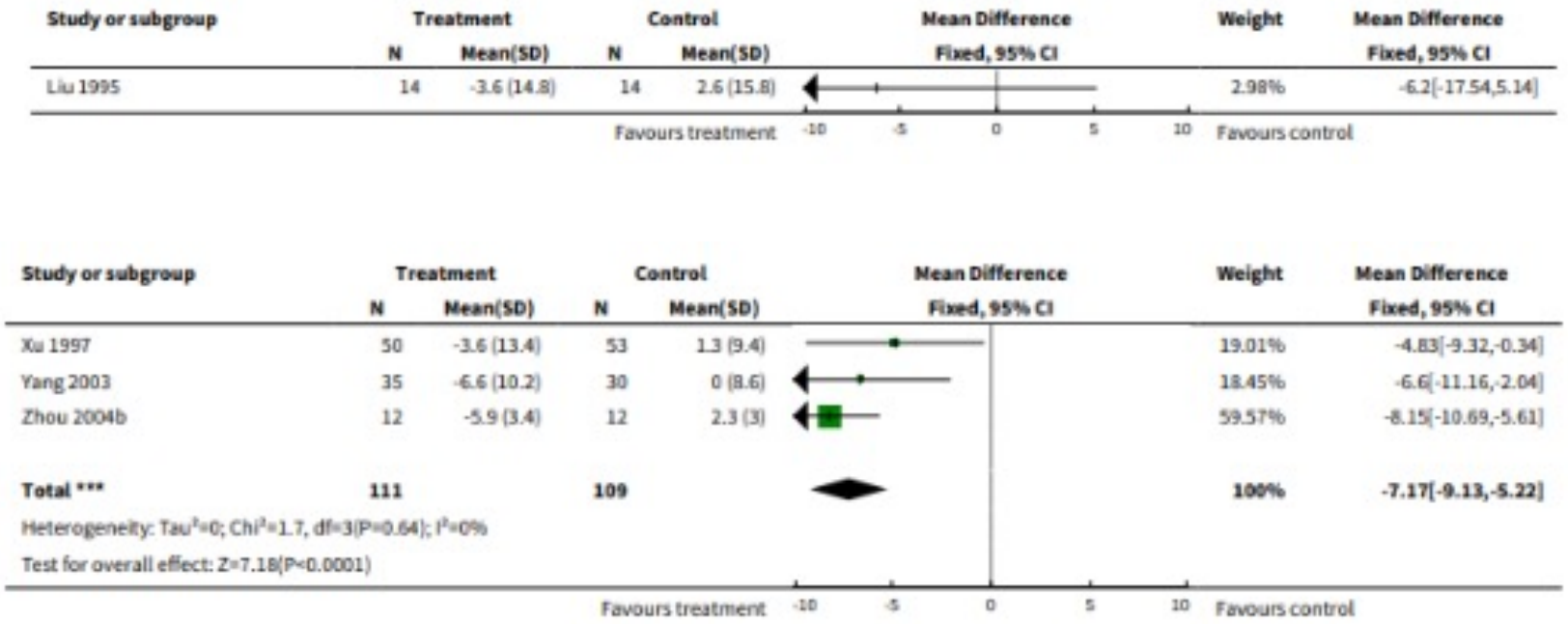
Favours control

Favours treatment

WILLPHARMA

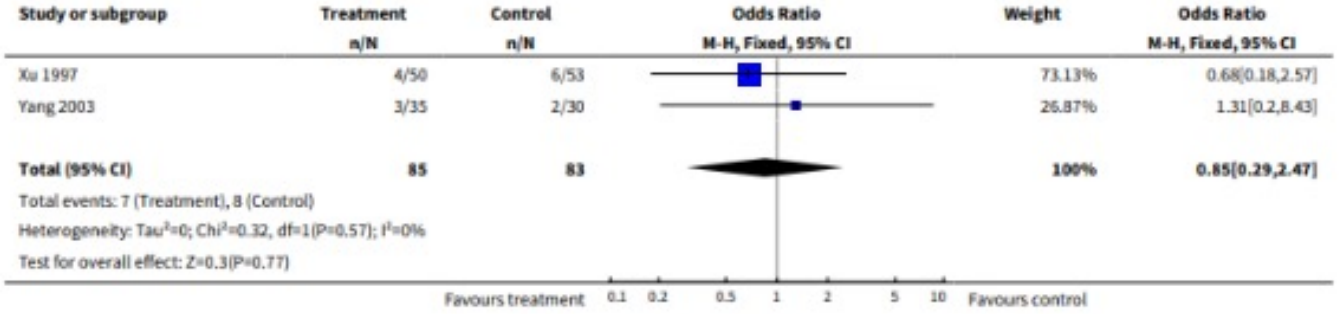
Cochrane Review

Analysis 1.4. Comparison 1 Huperzine A versus placebo only, Outcome 4 The change of functional performance measured by ADL at the end of treatment.

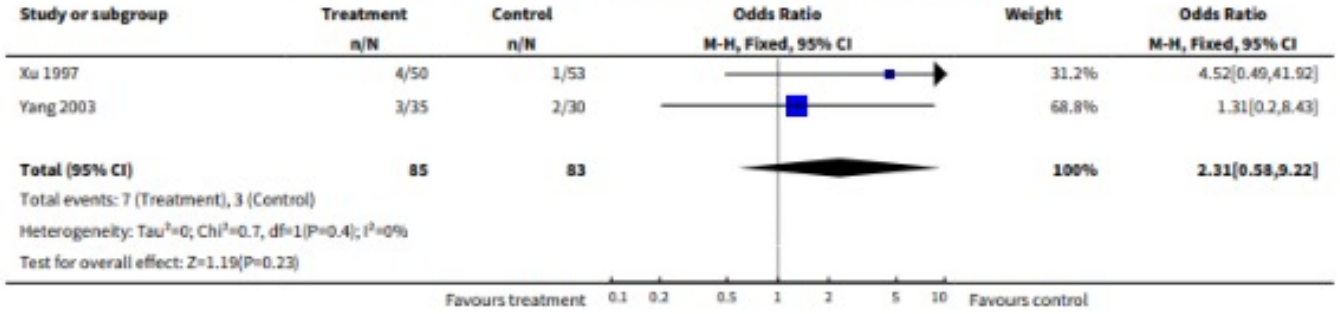


Cochrane Review

Analysis 1.6. Comparison 1 Huperzine A versus placebo only, Outcome 6 The number of dizziness during the treatment period.



Analysis 1.7. Comparison 1 Huperzine A versus placebo only, Outcome 7 The number of nausea or vomiting during the treatment period.



CBIP- Fiche transparence “Démence”

Fiche démence - CBIP

- Traitement médicamenteux de la démence 2011 (p.44)

Huperzine A

Pour la première fois, l'efficacité du médicament chinois 'huperzine A' a été étudiée en dehors de la Chine chez des personnes présentant une forme légère à modérément sévère de démence. Il ressort d'une étude de phase II randomisée en double aveugle, contrôlée par placebo, qu'après un traitement de 16 semaines, la plus faible dose étudiée (200 µg 2 fois par jour) n'était pas efficace; en revanche, la dose plus élevée (400 µg 2 fois par jour) était associée à un effet positif limité mais significatif sur la cognition. Pour les autres critères d'évaluation, on n'a pas observé de différences significatives entre l'huperzine A (les deux doses) et le placebo. Il n'y avait pas de différence significative en ce qui concerne l'apparition d'effets indésirables[a].

a. Dans cette étude de phase II randomisée en double aveugle, 210 patients présentant une forme légère à modérément sévère de démence ont été randomisés en 3 groupes (huperzine A 200 µg 2 fois par jour, huperzine A 400 µg 2 fois par jour et un placebo). Après 16 semaines de traitement, seul le groupe ayant reçu la dose la plus élevée manifestait une différence limitée mais significative par rapport au placebo en ce qui concerne la cognition: avec l'huperzine A 400 µg, on a constaté une amélioration de 1,1 points sur le MMSE, par rapport à une diminution de 0,4 points dans le groupe placebo (p = 0,007); les résultats sur l'ADAS-Cog étaient tout juste non significatifs. On peut douter de l'impact clinique de cette différence limitée. La plus faible dose n'était pas associée à un effet significatif sur la cognition. On n'a pas observé de différences entre les deux groupes d'intervention et le groupe placebo en ce qui concerne le comportement, les AVQ et l'impression d'amélioration selon l'investigateur, ni en ce qui concerne l'apparition d'effets indésirables[12].

Rafii et al.

A phase II trial of huperzine A in mild to moderate Alzheimer disease

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ABSTRACT

Objective: Huperzine A is a natural cholinesterase inhibitor derived from the Chinese herb *Huperzia serrata* that may compare favorably in symptomatic efficacy to cholinesterase inhibitors currently in use for Alzheimer disease (AD).

Methods: We assessed the safety, tolerability, and efficacy of huperzine A in mild to moderate AD in a multicenter trial in which 210 individuals were randomized to receive placebo (n = 70) or huperzine A (200 μg BID [n = 70] or 400 μg BID [n = 70]), for at least 16 weeks, with 177 subjects completing the treatment phase. The primary analysis assessed the cognitive effects of huperzine A 200 μg BID (change in Alzheimer's Disease Assessment Scale–cognitive subscale [ADAS-Cog] at week 16 at 200 μg BID compared to placebo). Secondary analyses assessed the effect of huperzine A 400 μg BID, as well as effect on other outcomes including Mini-Mental State Examination, Alzheimer's Disease Cooperative Study–Clinical Global Impression of Change scale, Alzheimer's Disease Cooperative Study Activities of Daily Living scale, and Neuropsychiatric Inventory (NPI).

Results: Huperzine A 200 μg BID did not influence change in ADAS-Cog at 16 weeks. In secondary analyses, huperzine A 400 μg BID showed a 2.27-point improvement in ADAS-Cog at 11 weeks vs 0.29-point decline in the placebo group ($p = 0.001$), and a 1.92-point improvement vs 0.34-point improvement in the placebo arm ($p = 0.07$) at week 16. Changes in clinical global impression of change, NPI, and activities of daily living were not significant at either dose.

Rafii et al.

- Dosage : 2x400 µg/jour

RAFII ET AL. (N=210) (16WEEKS)

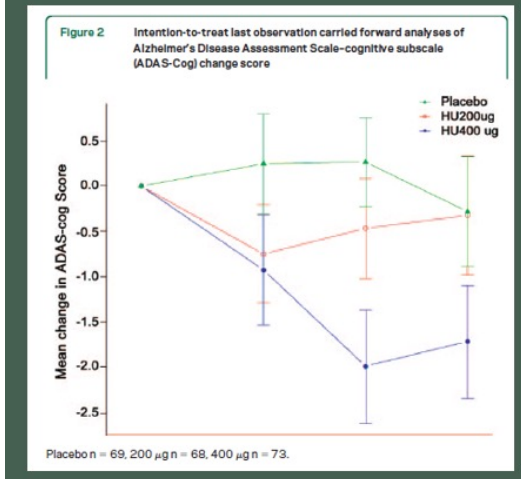

Table 3 Changes from baseline in cognitive and functional measures by treatment arm, at each timepoint, using last observation carried forward

Cognitive measure	Week 6 (SD)	Week 11 (SD)	Week 16 (SD)	p Value[a]
ADAS-Cog				
Placebo	0.25 (4.67)	0.29 (4.19)	−0.34 (5.17)	
200 µg	−0.75 (4.42)	−0.47 (4.51)	−0.32 (15.37)	0.980
400 µg	−0.93 (5.00)	−2.27 (5.11)	−1.92 (5.30)	0.070
MMSE				
Placebo	−0.33 (3.31)	0.12 (3.02)	−0.40 (3.31)	
200 µg	0.66 (2.85)	0.51 (2.91)	0.65 (2.85)	0.060
400 µg	0.91 (2.53)	1.03 (2.64)	1.10 (2.84)	0.007

Rafii et al.

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Li et al.

Longue Action

- 40 mg HSE = 400 µg HA

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Pharmacokinetics of huperzine A following oral administration to human volunteers

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PHARMACOKINETICS (LI ET AL)

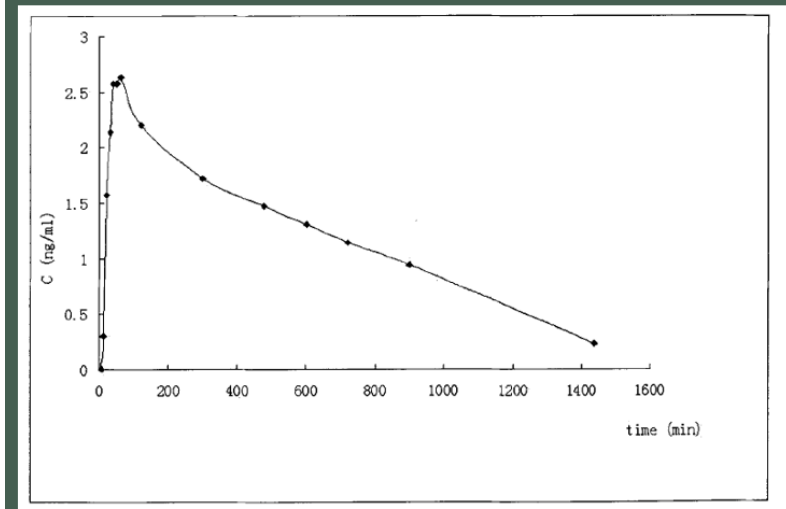

Figure 1. Mean plasma concentration time profile after oral administration of 0.4 mg of huperzine A in tablet form

1*0,4mg
⇒ 24h in blood
⇒ Start after 5-10minutes
⇒ Peak at +/- 1h
⇒ Elimination t1/2= 716min

Annexes

- GINKGO BILOBA

- Kennedy et al. (2007)
- Briskey and Rao (2022)

- HUPERZIA SERRATA

- Friedli and Inestrosa (2021)
- Rafii et al.
- Fiche Transparence Démence
- Li et al. (2006)
- Cochrane Review (2008)

Thank you