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## SUPPORTING INFORMATION

# MULTICOMPONENT, FRAGMENT-BASED, SYNTHESIS OF POLYPHENOL-CONTAINING PEPTIDOMIMETICS AND THEIR INHIBITING ACTIVITY ON BETA-AMYLOID OLIGOMERIZATION

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### Additional biophysical assays on polyphenols

#### Solubility tests

The first biophysical analysis performed on the new polyphenols was the solubility in aqueous solution because the working condition is Phosphate Buffer Solution (PBS) at pH 7.4 to mimic the physiological environment. Almost all compounds showed low solubility in a range from 25 to 500  $\mu$ M in aqueous solution except **1g**, **1h**, **1j** and **1q**. To overcome this obstacle, we dissolved all samples in 100% dimethyl sulfoxide (DMSO). In this solvent new polyphenols result all fully soluble. To continue working in aqueous solution, DMSO samples were diluted in PBS at the desired concentration by keeping the 1% DMSO in the final solution. Together with the solubility analysis, the turbidity trend depending on the concentration of the samples was also investigated, in order to verify that the new polyphenols did not aggregate or form micelles as the concentration increases, precipitating in water solution. In the following Figures, the blue solid line represents the absorbance of the samples at their characteristic wavelength over the concentration increase. The dashed red line shows the turbidity of the polyphenols at 405 nm over the concentration increase. For compounds **1a** and **1b** only the absorbance experiments were carried out.





































S17








































S37

































S53











































Sample Name: FEF51










Sample Name: FEF97

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## Sample Name: FEF93

Colonna Phenyl C6 150x3mm 3um con precolonna, Campione: FEF93 (conc.:100ugr/ml MeOH), sequenza, flusso 0,34ml/m in, Vinj=5ul, Temp. 25°C Term.ON, Dad 220, 254, 300, 33 Onm, grad. A=CH3CN - B=H2O, Omin B=60%, 10min B=0%

## Injection Date : 5/16/2017 1:44:17 PM Seq. Line : 3 Sample Name : FEF93 Location : Vial 3 Acq. Operator : AeVeO Inj: 1 Acq. Instrument : stanza306new Inj Volume : 5 µl Acq. Method : C:\HPCHEM\1\METHODS\POLIFEN.M Last changed : 5/16/2017 12:31:23 PM by AeVeO Analysis Method : C:\HPCHEM\1\METHODS\POLIFEN.M Last changed : 5/17/2017 8:26:04 AM by AeVeO (modified after loading) DAD1 D, Sig=330,16 Ref=360,100 (LISSEQ\FEF93\_00.D) mAU ОН 175 -150 -125 -100 -HO ÓMe 75 -1q 50 -25 -610

Area Percent Report

Sorted By	: Signal					
Multiplier		:	1.0	000		
Dilution		:	1.0000			
Use Multiplier	\$	Dilution	Factor	with	ISTDs	

Signal 1: DAD1 D, Sig=330,16 Ref=360,100

Peak	RetTime	Type	Width	Area	Height	Area	
#	[min]		[min]	[mAU*s]	[mAU]	olo	
1	4.214	BB	0.1171	1499.56262	192.03836	99.3795	
2	6.610	PB	0.1039	9.36271	1.36681	0.6205	

Totals: 1508.92533 193.40517

Results obtained with enhanced integrator!