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Supporting Information

Pseudo Natural Products—Chemical Evolution of Natural Product Structure

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Author Contributions

G.K. performed the cheminformatic analyses. All authors wrote and commented on the manuscript.

Molecular properties were calculated using RDKit (http://www.rdkit.org) running in Python 3.7. Plots were generated using Matplotlib.[1]

Molecular properties of individual pseudo-NP classes used for the cheminformatic analyses:

Pyranofuranopyridones[2]

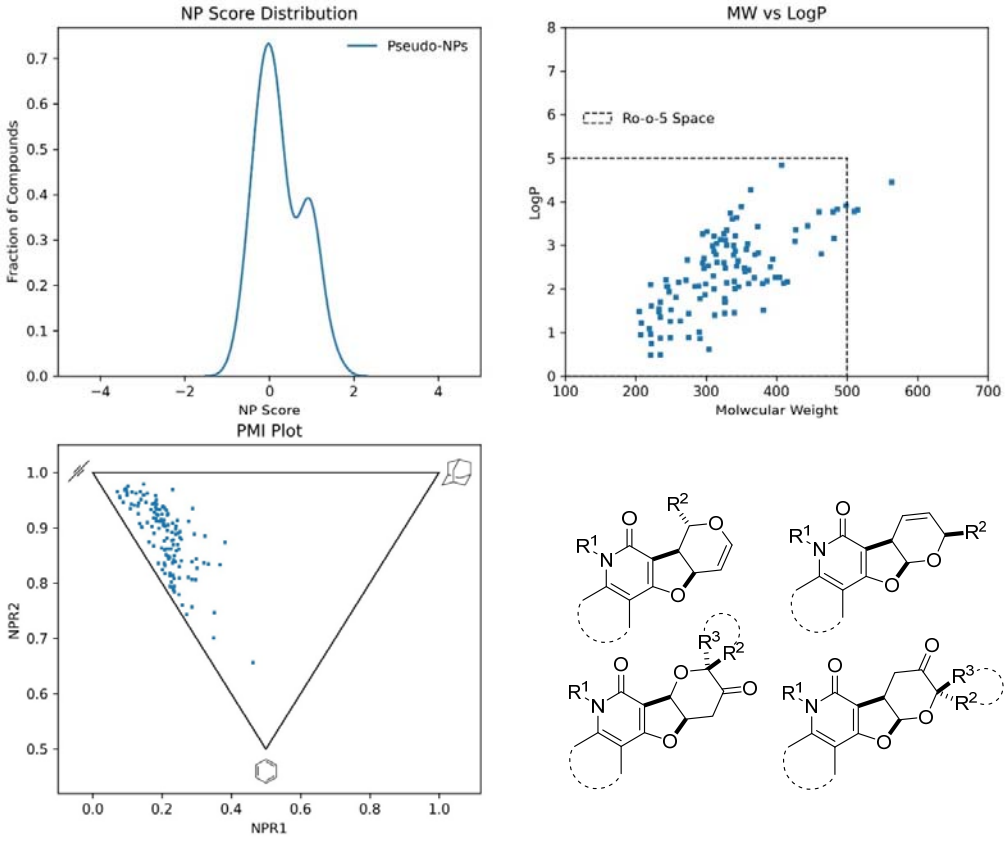

Figure S1: Molecular properties of pyranofuranopyridone pseudo-NPs. Top left: NP Score distribution. Top right: Molecular Weight against LogP. Dashed box denotes “Rule-of-five” space. Bottom left: PMI plot[3] of pyranofuranopyridone scaffold derivatives. Bottom right: Pyranofuranopyridone scaffolds structures.

Indomorphans[4]

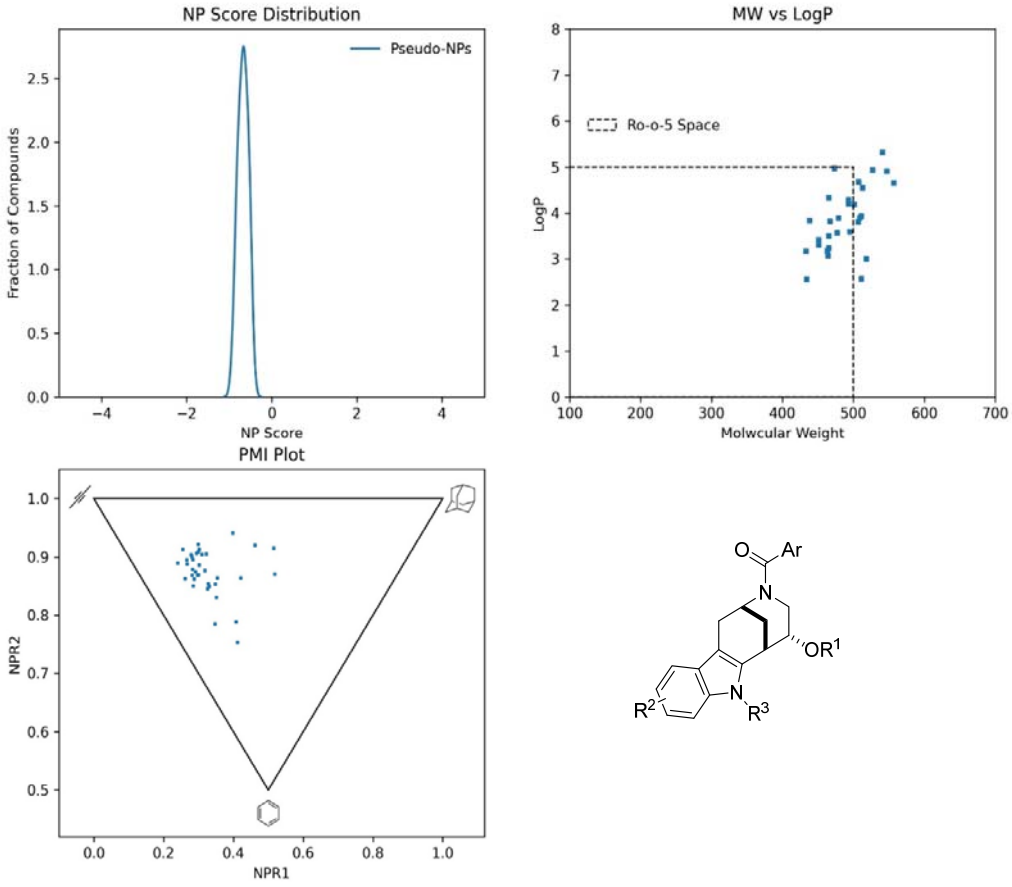

Figure S2: Molecular properties of indomorphan pseudo-NPs. Top left: NP Score distribution. Top right: Molecular Weight against LogP. Dashed box denotes “Rule-of-five” space. Bottom left: PMI plot[3] of indomorphan scaffold derivatives. Bottom right: Indomorphan scaffold structures.

Pyrroquinolines[5]

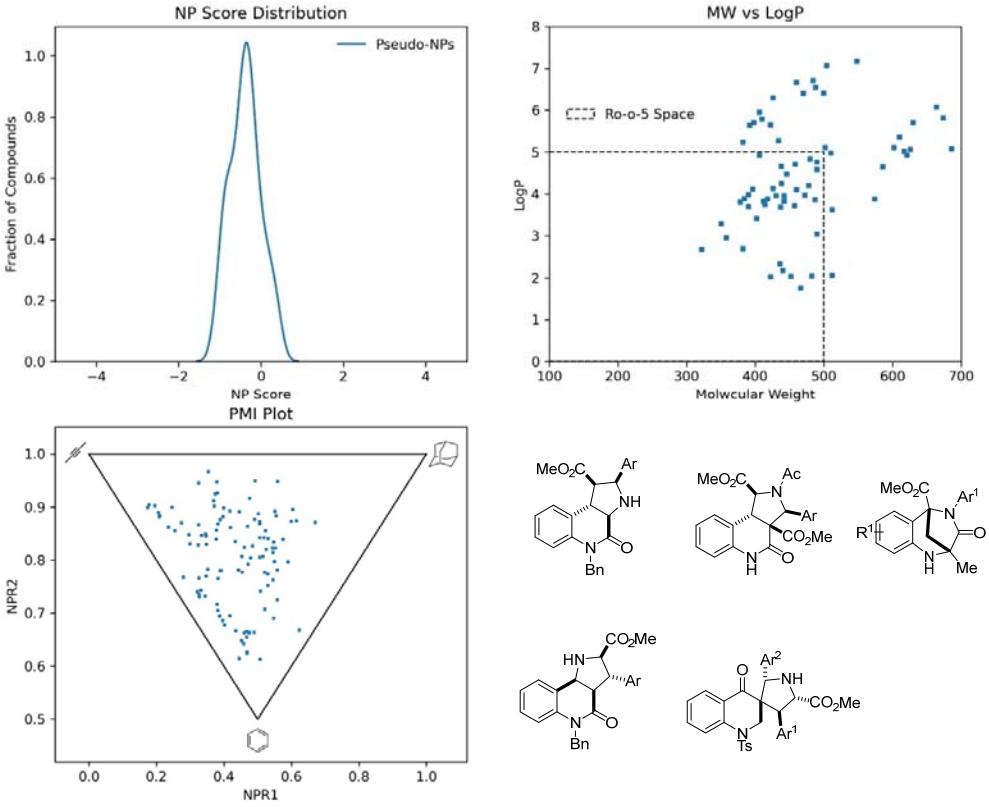

Figure S3: Molecular properties of pyrroquinoline pseudo-NPs. Top left: NP Score distribution. Top right: Molecular Weight against LogP. Dashed box denotes “Rule-of-five” space. Bottom left: PMI plot[3] of pyrroquinoline scaffold derivatives. Bottom right: pyrroquinoline scaffold structures.

Pseudo-NPs based on cinchona alkaloids[6,7]

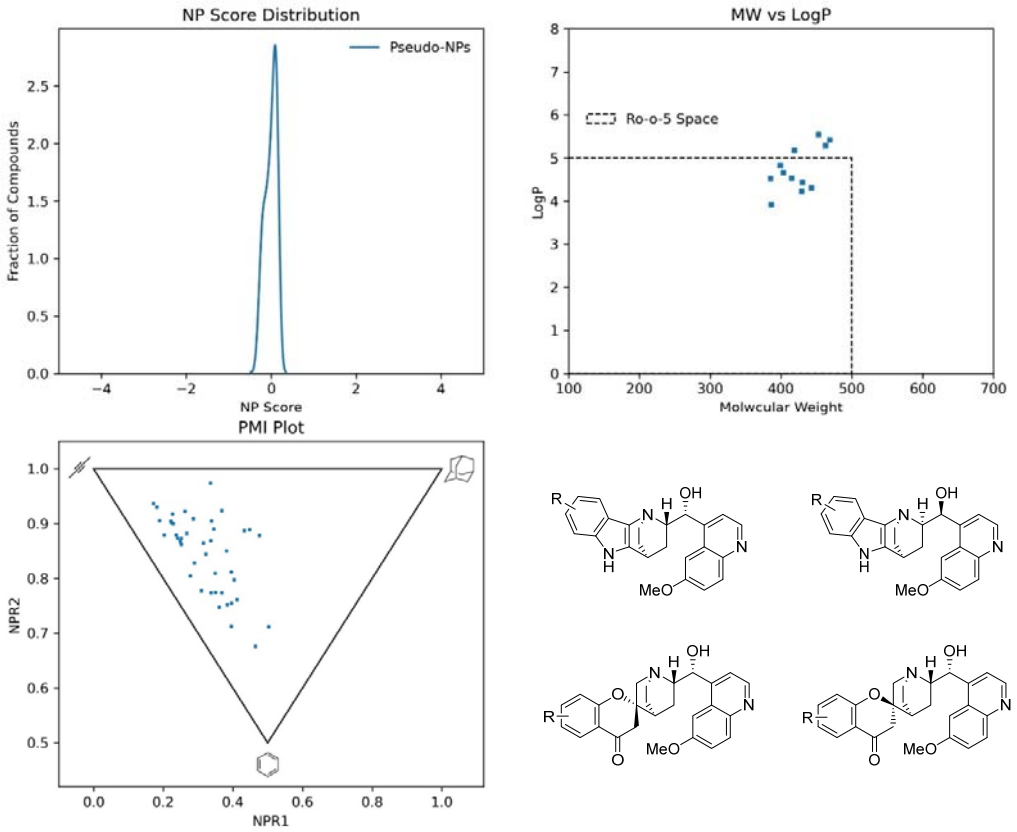

Figure S4: Molecular properties of cinchona pseudo-NPs. Top left: NP Score distribution. Top right: Molecular Weight against LogP. Dashed box denotes “Rule-of-five” space. Bottom left: PMI plot[3] of cinchona pseudo-NP derivatives. Bottom right: cinchona pseudo-NP scaffold structures.

Pseudo-NPs based on sinomenine, and griseofulvin[7]

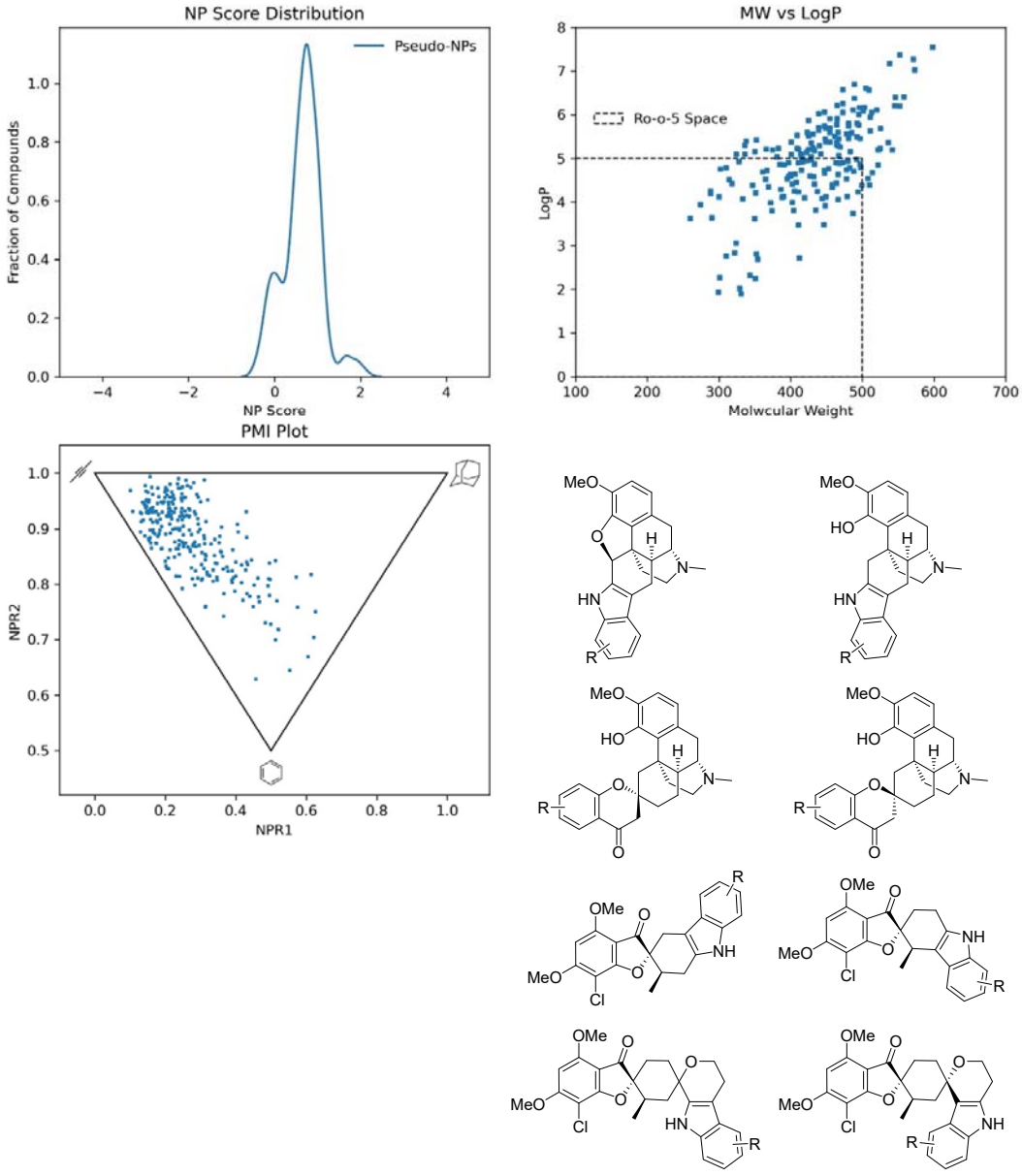

Figure S5: Molecular properties of sinomenine, and griseofulvin pseudo-NPs. Top left: NP Score distribution. Top right: Molecular Weight against LogP. Dashed box denotes “Rule-of-five” space. Bottom left: PMI plot[3] of sinomenine, and griseofulvin pseudo-NP derivatives. Bottom right: sineomenine, and griseofulvin pseudo-NP scaffold structures.

Chromopynones[8]

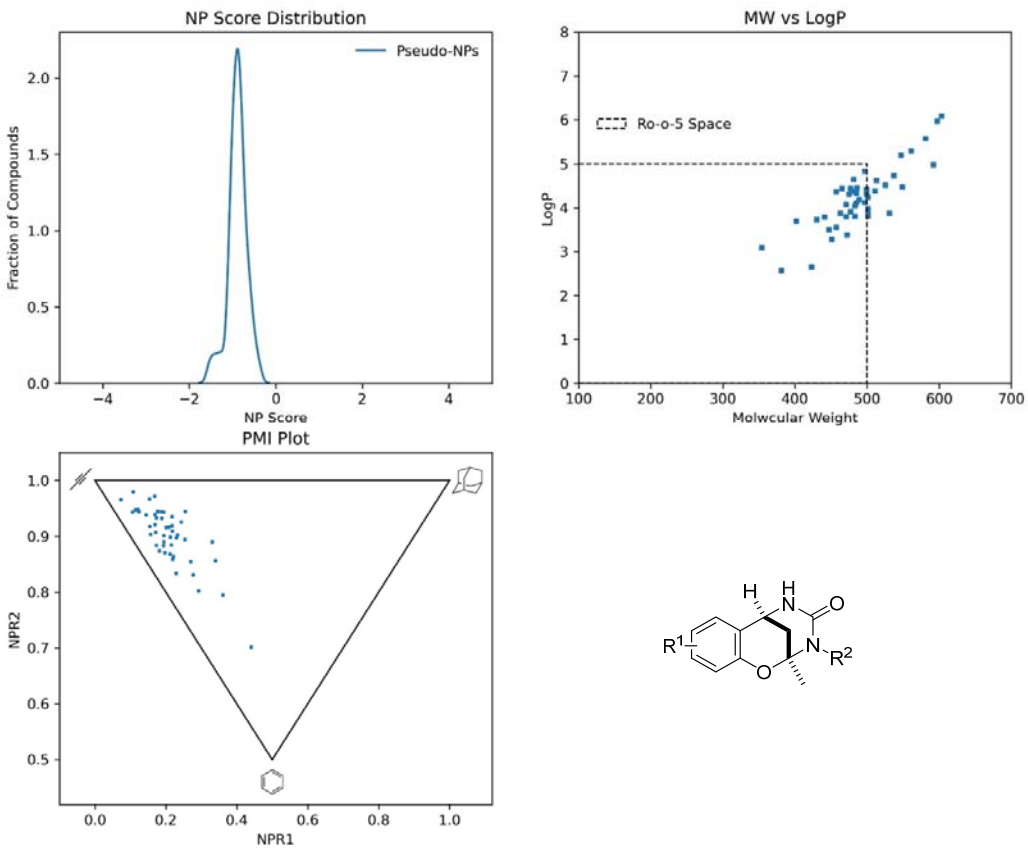

Figure S6: Molecular properties of chromopynone pseudo-NPs. Top left: NP Score distribution. Top right: Molecular Weight against LogP. Dashed box denotes “Rule-of-five” space. Bottom left: PMI plot[3] of chromopynone scaffold derivatives. Bottom right: chromopynone scaffold structure.

Table S1: Molecular properties of combined pseudo-NP libraries, averages and ranges.

	Mean	Range	Lit. Guidelines
Molecular Weight	426	205 - 686	150-500
LogP	4.26	0.47 - 7.61	0-5
Hydrogen-bond Acceptors	5	1 - 10	< 10
Hydrogen-bond Donors	1	0 - 3	< 5
Total Polar Surface Area ($Å^2$)	64	8 - 136	< 140
Fraction of sp^3 C atoms	0.36	0.08 - 0.72	0.3-0.6

Literature guidelines referred in literature[9–13]

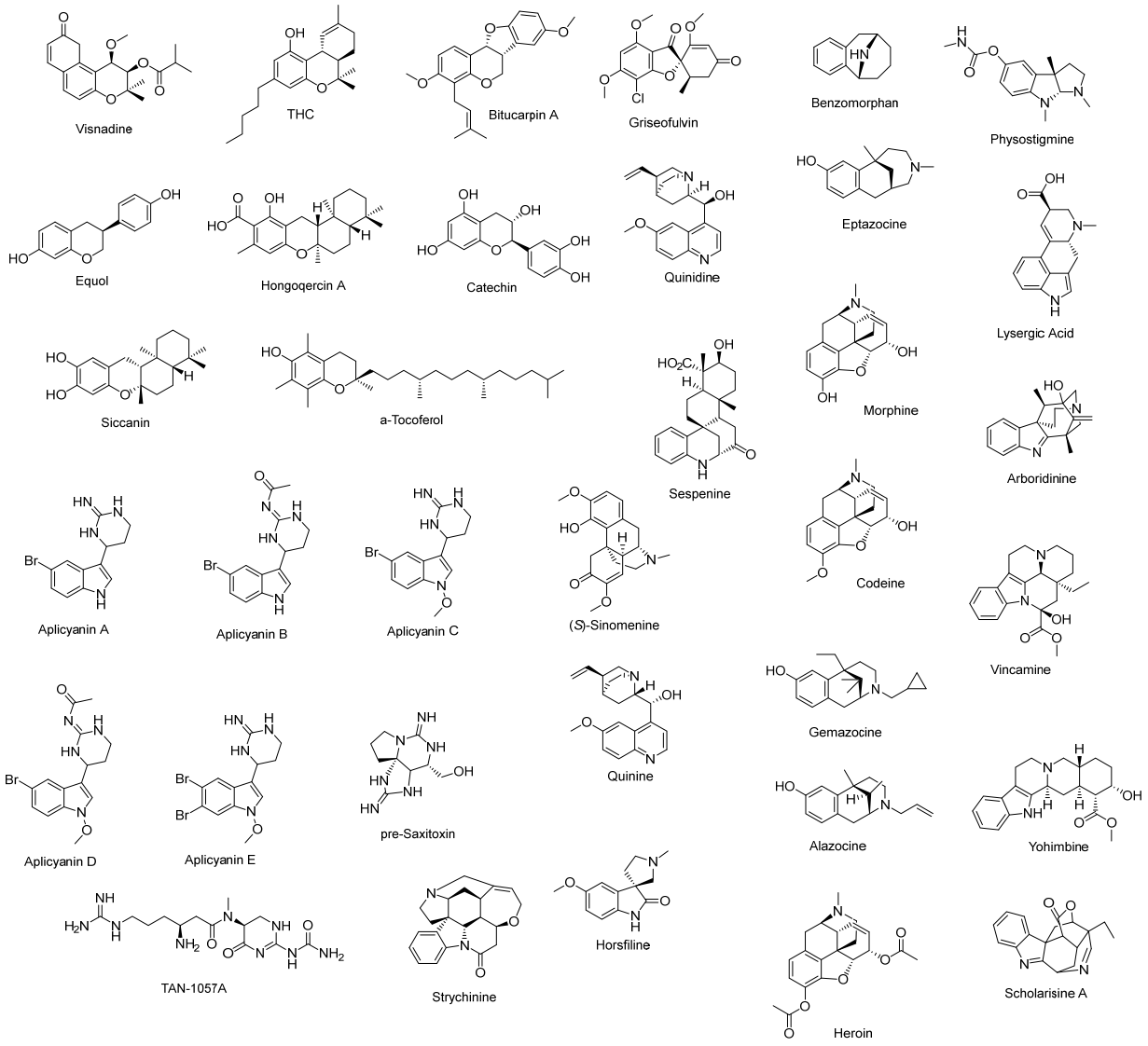

Figure S7: Structures and names for NPs and bioactive compounds used to prepare the PMI plot II in Figure 3.

References:

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