

## Supplementary Material

### Naphthoquinone as a new chemical scaffold for leishmanicidal inhibitors of *Leishmania* GSK-3

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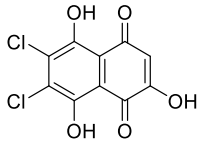
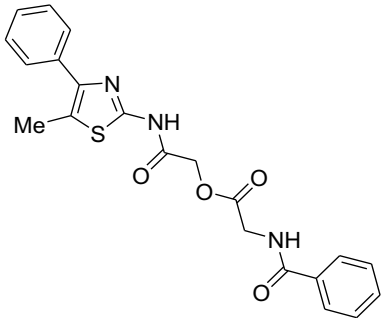
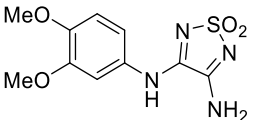
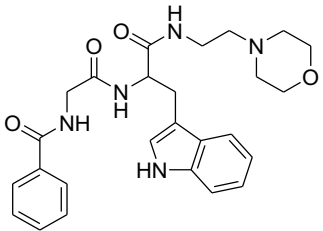
#### Index:

**Page S2:** Sequence alignment of the GSK-3 structures of *Leishmania major* (Q4QE15) and *Homo sapiens* (P49841).

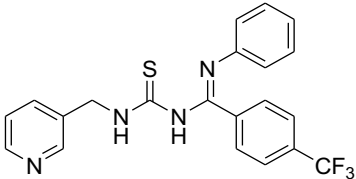
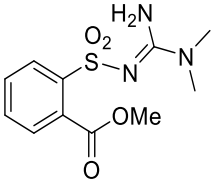
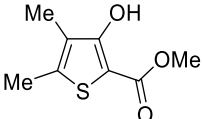
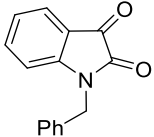
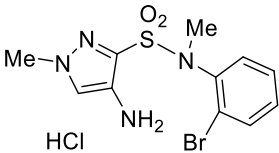
**Page S3:** Chemical structures of the 24 compounds from the MBC library selected by virtual screening and their biological evaluation.

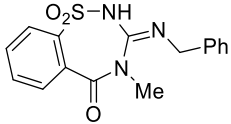
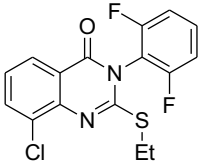
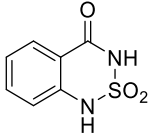
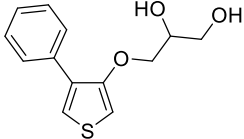
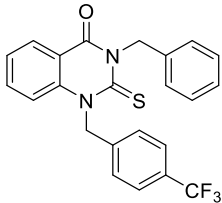


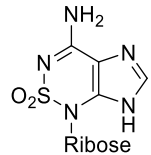
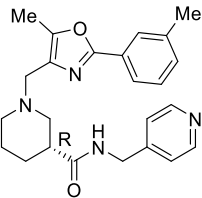
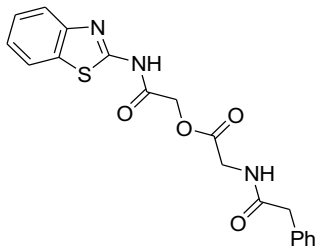
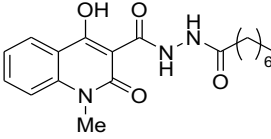
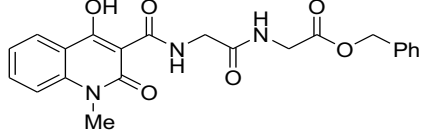
**Table S1.** Enzymatic and biological characterization of the 24 compounds from the MBC library selected by virtual screening.

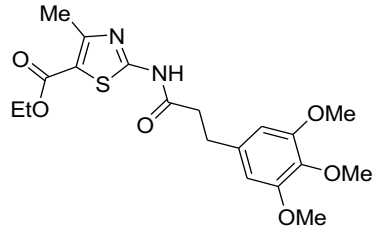
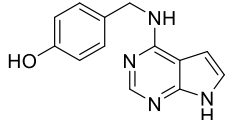
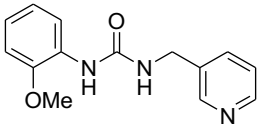
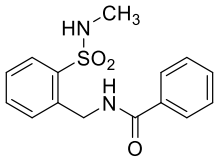
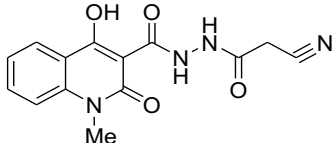
Compound	Chemical formula	LdGSK-3s IC <sub>50</sub> (μM)	<i>L. infantum</i> promastigotes IC <sub>50</sub> (μM)	<i>L. pifanoi</i> axenic amastigotes IC <sub>50</sub> (μM)	Murine peritoneal macrophages IC <sub>50</sub> (μM)	Selectivity index (SI)
MBC-10		~10*	10.5 ± 1.2	11.2 ± 2.5	ND	ND
MBC-49		>10	>50	>50	-	-
MBC-61		>10	>50	>50	-	-
MBC-85		>10	>50	>50	-	-

\* MBC-10 at 10 μM causes 45.7 ± 7.6 % inhibition of LdGSK-3s activity.

Compound	Chemical formula	LdGSK-3s IC <sub>50</sub> (μM)	<i>L. infantum</i> promastigotes IC <sub>50</sub> (μM)	<i>L. pifanoi</i> axenic amastigotes IC <sub>50</sub> (μM)	Murine peritoneal macrophages IC <sub>50</sub> (μM)	Selectivity index (SI)
MBC-11		>10	>25	>25	-	-
MBC-188		>10	>50	>50	-	-
MBC-189		>10	>50	>50	-	-
MBC-190		>10	>50	>50	-	-
MBC-191		>10	>50	>50	-	-

Compound	Chemical formula	LdGSK-3s IC <sub>50</sub> (μM)	<i>L. infantum</i> promastigotes IC <sub>50</sub> (μM)	<i>L. pifanoi</i> axenic amastigotes IC <sub>50</sub> (μM)	Murine peritoneal macrophages IC <sub>50</sub> (μM)	Selectivity index (SI)
MBC-192		>10	>50	>50	-	-
MBC-193		>10	>50	>50	-	-
MBC-194		>10	>50	>50	-	-
MBC-195		>10	>50	>50	-	-
MBC-196		>10	>25	>50	-	-

Compound	Chemical formula	LdGSK-3s IC <sub>50</sub> (μM)	<i>L. infantum</i> promastigotes IC <sub>50</sub> (μM)	<i>L. pifanoi</i> axenic amastigotes IC <sub>50</sub> (μM)	Murine peritoneal macrophages IC <sub>50</sub> (μM)	Selectivity index (SI)
MBC-197		>10	>50	>50	-	-
MBC-198		>10	>50	>50	-	-
MBC-199		>10	>50	>50	-	-
MBC-200		>10	>50	20.8 ± 0.0	>25	>1.2
MBC-201		>10	>50	>50	-	-

Compound	Chemical formula	LdGSK-3s IC <sub>50</sub> (μM)	<i>L. infantum</i> promastigotes IC <sub>50</sub> (μM)	<i>L. pifanoi</i> axenic amastigotes IC <sub>50</sub> (μM)	Murine peritoneal macrophages IC <sub>50</sub> (μM)	Selectivity index (SI)
MBC-202		>10	>50	>50	-	-
MBC-203		>10	>50	>50	-	-
MBC-204		>10	>50	>50	-	-
MBC-205		>10	>50	>50	-	-
MBC-206		>10	>50	>50	-	-