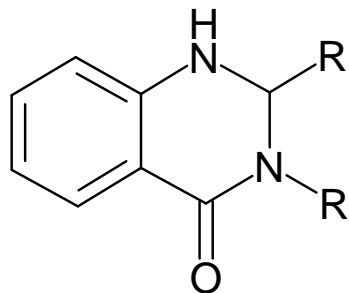


DIHYDROQUINAZOLINONE FOCUSED LIBRARY

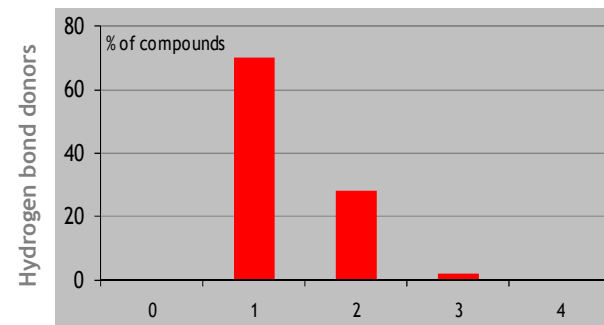
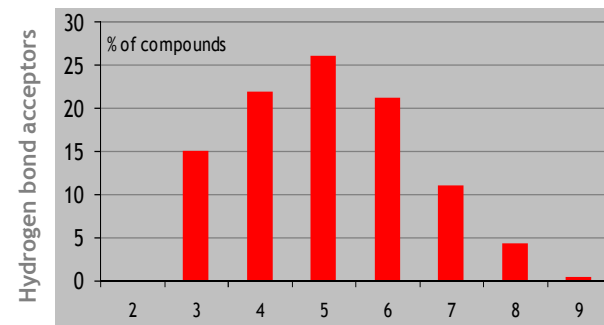
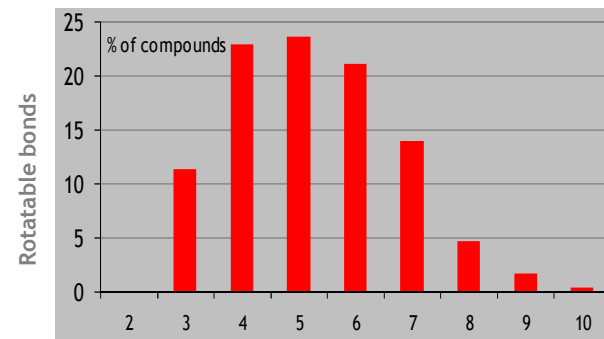
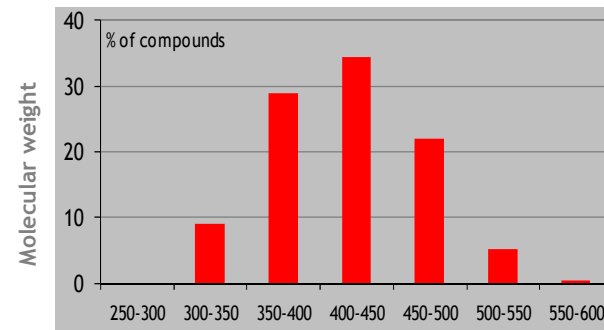
The scaffold:



Bullet points:

- * highly diverse exploration of dihydroquinazolinones
- * focused library for first intention screening
- * systematic variations for preliminary SAR establishment
- * privileged structures for diuretics, analgesics, antibiotics, anti-tumoral compounds with largely unexplored pharmacology
- * drug-like structures with reported oral and CNS activities
- * systematic LC/MS preparative purification
- * 550+ compounds with high diversity
- * cherry-picking and custom format available

CHARACTERISTIC CHARTS



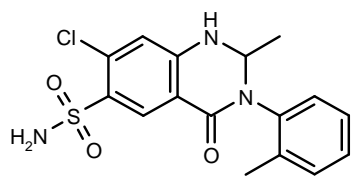
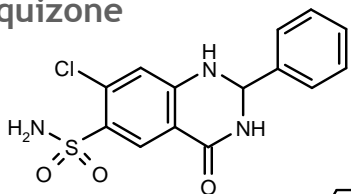
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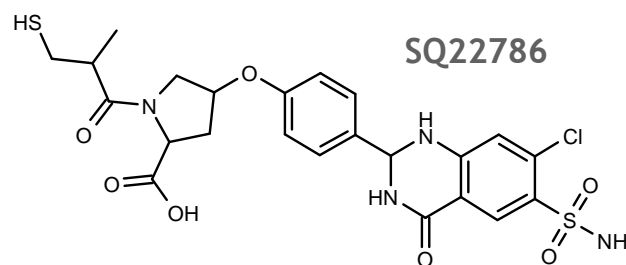
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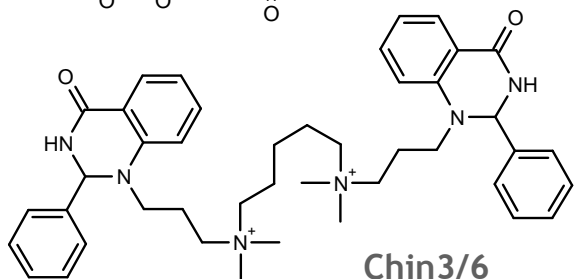
Fenquizone



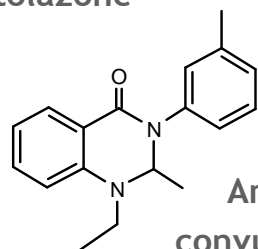
Metolazone



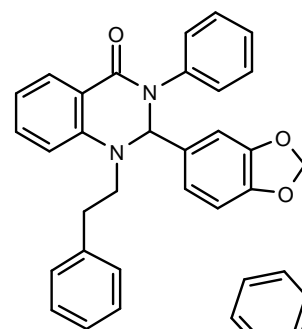
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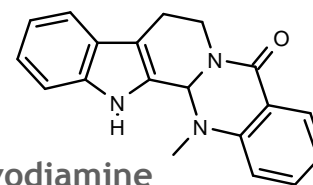
Chin3/6



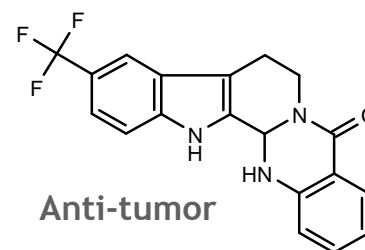
Anti convulsive



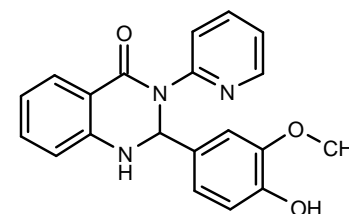
Analgesic



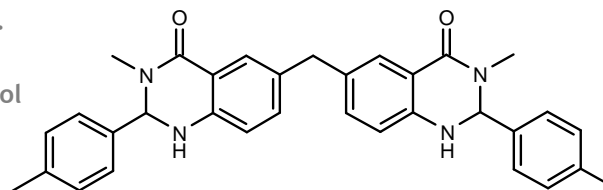
Evodiamine



Anti-tumor



Antibiotics



Isatoic anhydride is a versatile building block for combinatorial chemistry. Chem-X-Infinity has adapted a two step connecting chemistry to produce a library of 2,3-substituted dihydroquinazolinones¹. The anhydride is opened with a large diversity of amines. Then cyclisation of the obtained aminoamide with diverse aldehydes provided the heterocycle.

The dihydroquinazolinone scaffold is well represented in marketed drugs such as the thiazide diuretics Fenquizone and Metolazone, which are orally active Na⁺ Cl⁻ symporter inhibitors. SQ22786 has been developed as a mixed angiotensin-converting enzyme inhibitor diuretics.

The dihydroquinazolinone scaffold is also present in several compounds with reported CNS and *in vivo* activities. Chin3/6 has been studied as an allosteric muscarinic modulator more stable than the corresponding di-phthalimide derivative². Anti-convulsive properties have been described in mice for simple N-3-aryl derivatives³. N-1-phenethyl derivatives have been characterized as orally active potent analgesics and anti-inflammatories in mice⁴.

Evodiamine, a compound isolated from a Chinese herbal drug named Wu-Chu-Yu, has been reported to exhibit anti-tumor growth and metastasis as well as anti-tubulin and anti-angiogenic properties which may be due the inhibition of VEGF expression. Evodiamine represents a highly promising chemotherapeutic agent superior to Paclitaxel against the human multiple-drug resistant tumor xenograft⁵. Analogues of Evodiamine have been found active in HT-29 colon cancer xenografts⁶. 2- aryl derivatives have also been described as antibiotics^{7,8}.

We believe that Chem-X-Infinity's dihydroquinazolinone library is an efficient tool for the exploration of this versatile pharmacophore, and will be of great help for the discovery of new leads in a large array of therapeutic fields.



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¹ *J. Med. Chem.*, **1970**, *13*, 329

² *J. Pharm. Pharmacol.*, **1994**, *46*, 108

³ *Pharm. Chem. J.*, **1981**, *15*, 403

⁴ *Eur. J. Med. Chem.*, **1987**, *22*, 169

⁵ *Carcinogenesis*, **2005**, *26*, 968

⁶ *Bioorg. Med. Chem.*, **2004**, *12*, 1991

⁷ *Pharm. Chem. J.*, **1984**, *18*, 702

⁸ *Indian J. Chem. Sect. B*, **2002**, *11*, 2405