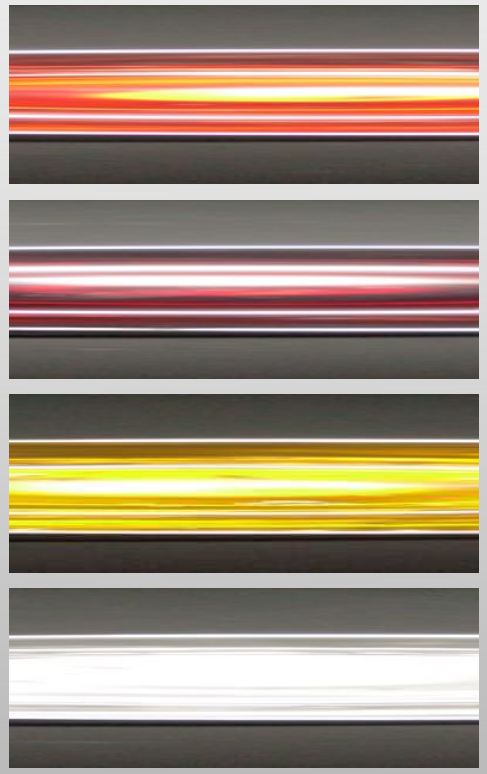
CHEM-X INFINITY



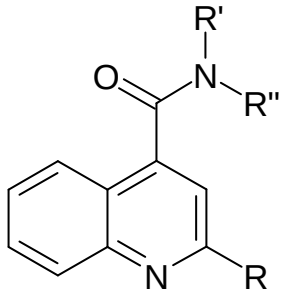
102 avenue Gaston Roussel
93230 - ROMAINVILLE - France

+33 1 41 83 02 03
+33 1 41 83 02 04 (fax)

www.chem-x-infinity.com

QUINOLINE CARBOXAMIDES

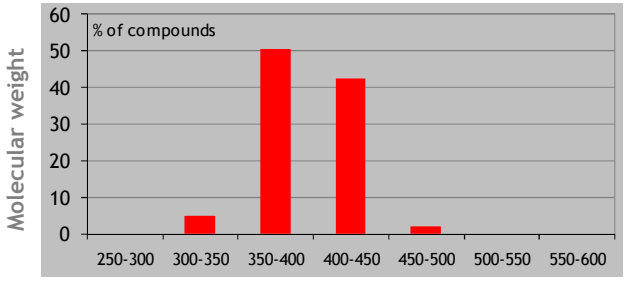
The scaffold:

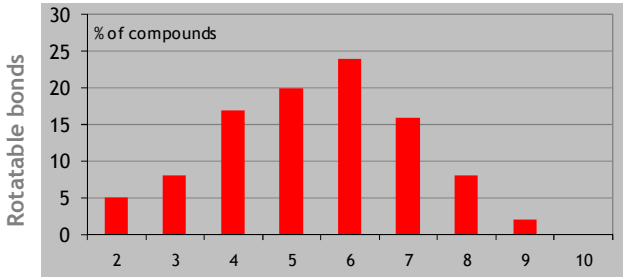


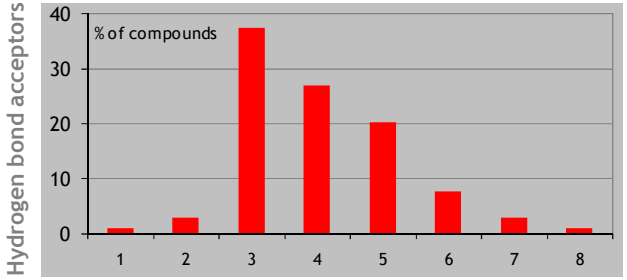
Bullet points:

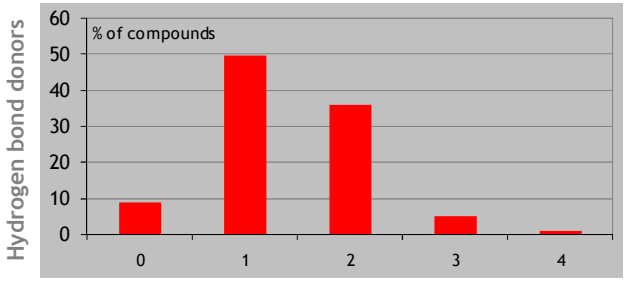
* first-line and diverse library exploring the quinoline carboxamide privileged structure
* open scaffold from a structural point of view allowing fast synthesis of focused libraries
* wide pharmacological spectrum: peptide and amine GPCRs, protein-protein interactions, ion channels and enzyme inhibitors
* many different therapeutic fields including cancer, analgesia and CNS, immunology, cardiovascular, gastrointestinal and pulmonary
* oral activities reported for similar structures
* 800+ compounds based on 16 intermediates
* cherry-picking and custom format available

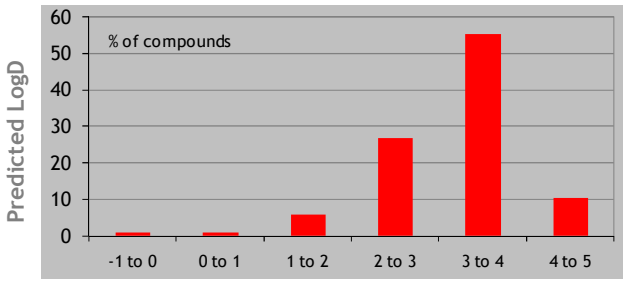
CHARACTERISTIC CHARTS

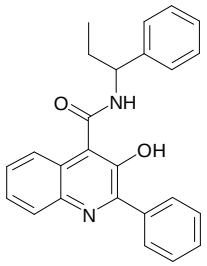




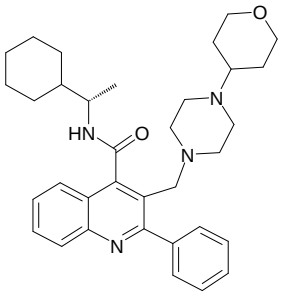




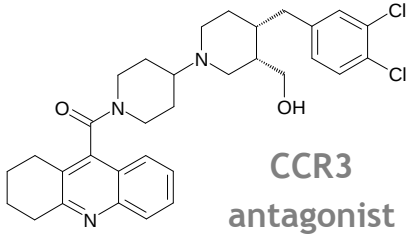




Talnetant

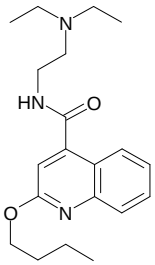


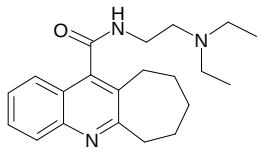
NK2/NK3 antagonist



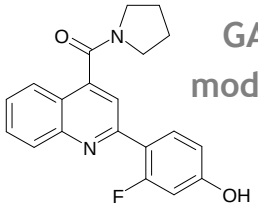
CCR3 antagonist

Dibucaine

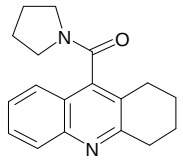




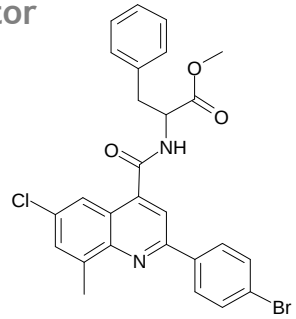
Antiarrhythmic



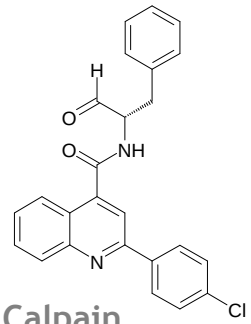
$GABA_A$ modulator



Analgesic



Prolyl-tRNA synthetase inhibitor

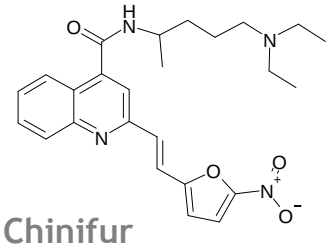


Calpain inhibitor

Chem-X-Infinity's quinoline carboxamide library has been designed to give the medicinal chemists an efficient tool for the exploration of a versatile pharmacophore which has found use in a wide spectrum of medicinal targets: GPCRs, protein-protein interactions, ion channels and enzyme inhibitors.

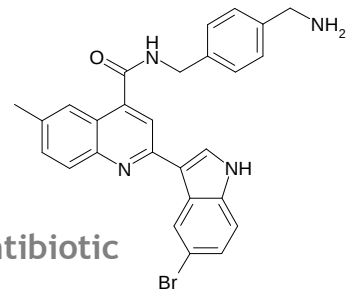
The term "privileged structures" was first used in 1988 by Evans *et al.*[1] and has since received general acceptance in medicinal chemistry. Chem-X-Infinity's scientists have selected quinoline carboxamide as a particularly interesting privileged medicinal structure covering a surprisingly wide pharmacological spectrum. For instance, many quinoline carboxamide derivatives have been developed as peptide GPCR antagonists. Talnetant is a selective and orally active NK3 antagonist which has been studied for urinary incontinence and irritable bowel syndrome. Small changes in the structures resulted in mixed NK2/NK3 antagonists[2]. Other examples of quinolines have been described for CCR3[3], CCR5, substance P, NPY5 and VCAM inhibition.

Applications in ion channels are also described. Dibucaine is an analgesic sodium channel blocker used for spinal analgesia. Related fused quinoline carboxamides have been described as antiarrhythmics and analgesics[4]. Simple 2-aryl quinoline carboxamides acting through $GABA_A$ receptors have been patented as tranquillizers[5].



Chinifur

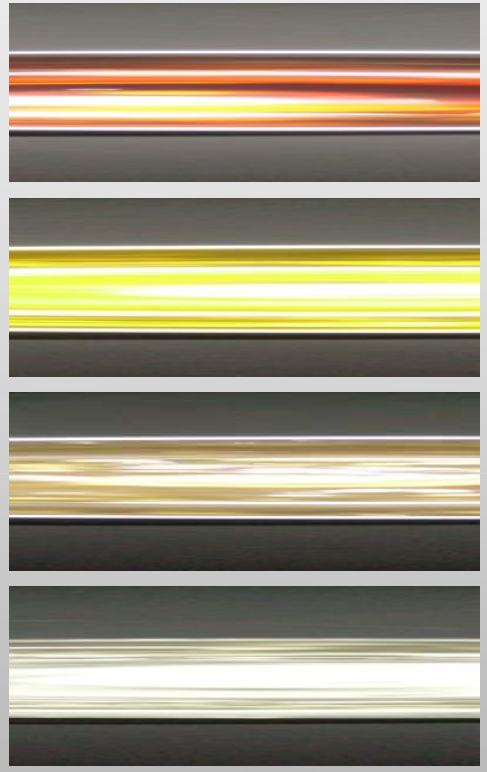
Quinoline carboxamides can also inhibit enzymes. 2-aryl-4-carboxamide quinoline was described as prolyl-tRNA synthetase inhibitor with high specificity for bacterial enzymes[6]. Similar compounds have been described as inhibitors of the calcium dependant proteolytic enzyme calpain[7]. Chinifur is a selective inhibitor of trypanosome trypanothione reductase, acting as a competitive inhibitor of NADPH[8].



Antibiotic

Finally, 2-indolyl-quinoline-4-carboxamides have been described as a novel structural class of antibiotics with activity on methicillin resistant strain[9].

CHEM-X INFINITY



[1] *J. Med. Chem.*, **1988,** *31,* 2235
[2] *J. Med. Chem.*, **2001,** *44,* 1675
[3] *US2005182095*
[4] *Indian J. Chem. Sect. B,* **1987,** *26,* 318
[5] *WO 0214269*
[6] *Bioorg. Med. Chem. Lett.*, **2001,** *11,* 541
[7] *WO9841506*
[8] *Bioch. Bioph. Res. Comm.*, **1994,** *204,* 224
[9] *WO9857952*