Future Medicinal Chemistry

Topological Index Nclass as a factor determining the antibacterial activity of quinolones against Escherichia coli.

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1   **ABSTRACT.**

2   **Background:** Due to antibiotic resistance and the lack of investment in

3   antimicrobial R&D, QSAR methods appear as an ideal approach for the discovery of new

4   antibiotics. **Result/Methodology:** Molecular topology and LDA were used to construct

5   a model to predict activity against *Escherichia coli*. This model establishes new SARs, of

6   which, molecular size and complexity (*Nclass*), stand out for their discriminant power.

7   This model was used for the virtual screening of the Index Merck database, with results

8   showing a high success rate as well as a moderate restriction. **Conclusions:** The model

9   efficiently finds new active compounds. The topological index *Nclass* can act as a filter

10   in other QSAR models predicting activity against *E. coli*.

11

12   **KEY WORDS.** Quinolones, Antibacterial activity, QSAR, Molecular Topology, *Escherichia*

13   *coli*

14

15   **INTRODUCTION.**

16   In the early 60s, a group of experts in infectious diseases announced the need to

17   accelerate the discovery of new antibacterial drugs due to the increasing resistance of

18   some bacteria, such as pneumococci or staphylococci, against traditional antibiotics [1].

19   Since then, the scientific community has witnessed how the number of antibiotic

20   resistant bacteria has increased exponentially during the last few decades. In fact,

21   according to WHO (World Health Organization) estimates, if resistances continue to

22   increase at the present rate, infectious diseases will become the first cause of death

23   worldwide with more than 10,000,000 deaths, exceeding those caused by cancer,

24   diabetes and cardiovascular diseases [2].

25   *Escherichia coli* is one of the bacterial species against which the development of

26   new antibiotics is crucial. In fact, WHO classifies it as a Priority 1 (Critical) pathogen in

27   their Priority Pathogens List of R&D of New Antibiotics [3]. *E. coli* is a usual commensal

28   in the gastrointestinal tract, which coexists symbiotically with its host [4]. However,

29   certain strains have acquired virulence factors that increase their ability to adapt to new

30   niches, allowing them to cause a broad spectrum of diseases [5]. Generally, these

31   diseases are grouped in three types: enteric, urinary tract infection or septicemia. The

32 development of resistances in this species is especially serious, having detected *E. coli*

33 strains resistant to all the antibiotics currently available, including colistin [6].

34 This increase in resistant strains necessitates the research of new antimicrobial

35 agents in order to increase the therapeutic arsenal. However, WHO has emphasized

36 repeatedly the insufficient investment currently dedicated to the development of

37 antimicrobial drugs [7]. The fact that antibiotics are used for acute treatments of short

38 duration and that, due to resistances, they lose efficacy a few years after they are

39 introduced in the market, has led the pharmaceutical industry to abandon all efforts of

40 developing new antimicrobial compounds. As a result, the discovery of new antibacterial

41 therapies relies on research centers and universities [8]. This is where QSAR

42 (Quantitative Structure-Activity Relationship) methods play a key role, seeing as they

43 provide useful information for the rational design of new molecules at a minimum cost

44 [9]. **With these methods, one can predict the pharmacological activity of a compound**

45 **without synthesizing it. Therefore, Computational Chemistry and Virtual**

46 **Combinatorial Chemistry** have experienced a great surge for the last few years [10, 11].

47 Since virtual libraries are usually big, filters are usually applied to discard molecules with

48 low probability of becoming drugs. Lipinski was the first to apply these filters by

49 describing the "rule of 5" in 1997 [12].

50 **QSAR methods have been used to study antibacterial activity against *E. coli* in**

51 **different ways. Some studies use known antibiotic families to obtain models for a**

52 **better understanding of the structural features that most contribute to antibacterial**

53 **activity against this microorganism [13,14]. For example, Cooper et al. developed a**

54 **model to identify physicochemical descriptors that best classify the potencies of ß-**

55 **lactams and fluoroquinolones against *E. coli* [13]. Similarly, Kawczack et al. revealed**

56 **influential features of fluoroquinolones for their activating against *E*. coli by**

57 **performing PCA and MLR on a set of these compounds [14]. On the other hand, the**

58 **most common application of QSAR models against *E. coli* is for the development of**

59 **new antibacterial compounds [15-17]. Along these lines, Merzoug et al. applied virtual**

60 **screening to a library of peptide deformylase inhibitors and found three peptides with**

61 **significant antibacterial activity and a novel mechanism of action [15]. Other studies**

62 **use QSAR models to obtain new compounds from families with known antibiotic**

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63 **activity, such as cinnamaldehyde-amino acid Schiff bases [16] and N-substituted**

64 **rhodanine synthons [17].**

65 The aim of this paper is to develop a prediction model to find new antibacterial

66 molecules and provide additional information regarding the possible structure-activity

67 relationships of quinolones.

68

69 **MATERIALS AND METHODS.**

70 *Compound selection*

71 Quinolones constitute a well-known therapeutic group commonly used for the

72 treatment of different infections, both in hospital and community settings. This group is

73 ideal for the development of a QSAR model because there is a great amount of

74 information published regarding active and inactive molecules within this family, which

75 is often the most difficult to find when conducting QSAR studies. This, along with the

76 fact that quinolones are generally safe and well tolerated drugs, is why they are ideal

77 candidates for the development of an antibacterial activity prediction model.

78 A group of 43 compounds with proven activity against *E. coli* was selected with a

79 literature search in ISI Web of Science, Medline and SciFinder. Furthermore, a group of

80 39 inactive compounds was also selected. **All 82 compounds had quinolone structure**

81 (the structure of all compounds as well as references regarding their activity can be

82 found in the Supporting Information file).

83 A compound was classified as active when it had a Minimum Inhibitory

84 Concentration (MIC) against *E. coli* ≤ 1mg/L. On the other hand, a compound was

85 classified as inactive when it had a MIC ≥ 16mg/L. Compounds with intermediate

86 activities (MIC > 1mg/L and MIC < 16mg/L) were not included in the compound

87 database. Regarding stereoisomers, only those compounds for which all stereoisomers

88 had the same activity were included in the database seeing as the descriptors used do

89 not include 3D parameters.

90

91 *Molecular connectivity and topological descriptors*

92 **The topological descriptors used are described in the Supporting Information,**

93 **as well as their definitions and references. A total of 148 descriptors were used to**

94 **characterize each compound. They were calculated using the hydrogen-depleted**

95 **graph to obtain the adjacency topological matrix with MOLCONN-Z [18] and**

96 **DESMOL13 [19] software.**

97

98 *Model construction*

99   *i.*   *Linear Discriminant Analysis*

100   Stepwise Linear Discriminant Analysis (LDA) was used in order to calculate 7

101 Discriminant Functions (DFs) using different combinations of the topological indexes (i.e.

102 electrotopological, electrotopological and charge, connectivity and charge, etc.). The

103 software used for the LDA was the BMDP 7M Biomedical package [20], which randomly

104 **selects molecules for the training and test groups. The topological indexes used to**

105 **calculate the linear classification functions were chosen in a stepwise manner using**

106 **the Fisher-Snedecor parameter, F, which determines the relationship between the**

107 **variance explained by the equation and the residual variance [21].**

108   **The discriminant power of the resulting equations was assessed by the**

109 **percentage of correct classifications for each group. The classification criterion is the**

110 **minimal Mahalanobis distance, which is the measure of the separation between the**

111 **active and inactive groups, this allowing to have an idea of the ability of the**

112 **discriminatory power of the final LDA model. The quality of the discriminant function**

113 **was assessed using the Wilk's U-statistical parameter, λ. LDA was then applied to the**

114 **training groups to obtain discriminant functions linking topological indexes and**

115 **antibacterial activity.**

116   Different combinations of the 7 DFs obtained were analyzed in order to obtain a

117 prediction model with one DF or the combination of several DFs with the best prediction

118 capability, especially of inactive compounds.

119

120   *ii.*   *Pharmacological Activity Distribution Diagrams*

121   **The pharmacological distribution diagrams (PDD) of the selected DFs were built**

122 **in order to determine the intervals of the DF with the maximum expectancy of finding**

123 **an active compound. PDDs are a type of histogram plot where connectivity functions**

124 **are represented with the expectancies on the ordinate axis. They allow the**

125 **visualization of regions of minimum overlap, allowing the selection of the intervals in**

126 **which the probability of finding active molecules is maximum [21].**

127   *Model validation (virtual screening)*

128   A virtual library was constructed based on the Index Merck database, which is

129   made up of more than 10000 compounds including drugs, biological products and

130   chemical reagents. All inorganic compounds and polymers were excluded. In the case of

131   stereoisomers, a single graph was drawn to represent all the different options. When an

132   organic cation corresponded to a conjugate acid, the corresponding base was drawn.

133   Anionic organic compounds were drawn as free acids.

134   Finally, the chemical graphs of 6384 compounds were drawn using

135   ChemBioDraw Ultra 12.0 and 148 topological indices were calculated for each

136   compound using DESMOL13 and MOLCONN-Z 3.0.

137

138   **RESULTS/DISCUSSION.**

139   *Prediction Model*

140   To obtain the DFs, a training group with 31 active and 32 inactive compounds

141   and a test group with 12 active and 7 inactive compounds were formed. The test group

142   allows the quality evaluation of the selected DFs. The selected discriminant functions,

143   DF1 and DF2, along with their corresponding statistical parameters are depicted in

144   equations 1 and 2 (the values for the indexes, DFs and classification probability along

145   with the activity classification of the compounds used for the construction of the model

146   can be found in the Supporting Information):

147

148   **DF1** = - 137.77814 + 13.66578$^5\chi_p$ − 9.46572$^0\chi_v$ + 14.55307SH_{tCH} − 3.10866$S_{>CH\text{-}}$ +

149   0.94222S_{Cl} − 6.32603$^4G^v$

150   N = 82   λ = 0.1230521   F = 66.515   (Eq. 1)

151   **DF2** = -108.72509 - 55.7222$^4\chi_c v$ - 0.91239N_{class} + 156.844^0C - 45.40381^2C

152   N = 82   λ = 0.2786756   F = 37.532   (Eq. 2)

153

154   Both equations have low values for λ, **which highlights that the linear**

155   **dependence between independent variables is not relevant. Furthermore, F presents**

156 **high values, indicating that the selected independent variables contribute largely to**

157 **the classification of both groups.**

158 In order for a compound to be considered active against *E. coli*, it had to have a

159 DF1 value between 0 and 32 and a DF2 value between 0 and 12. **On the other hand, to**

160 **avoid false actives, compounds with values for DF1 > 32 and/or DF2 > 12 are**

161 **considered unclassifiable These intervals were determined using the corresponding**

162 **PDDs (Figure 1).**
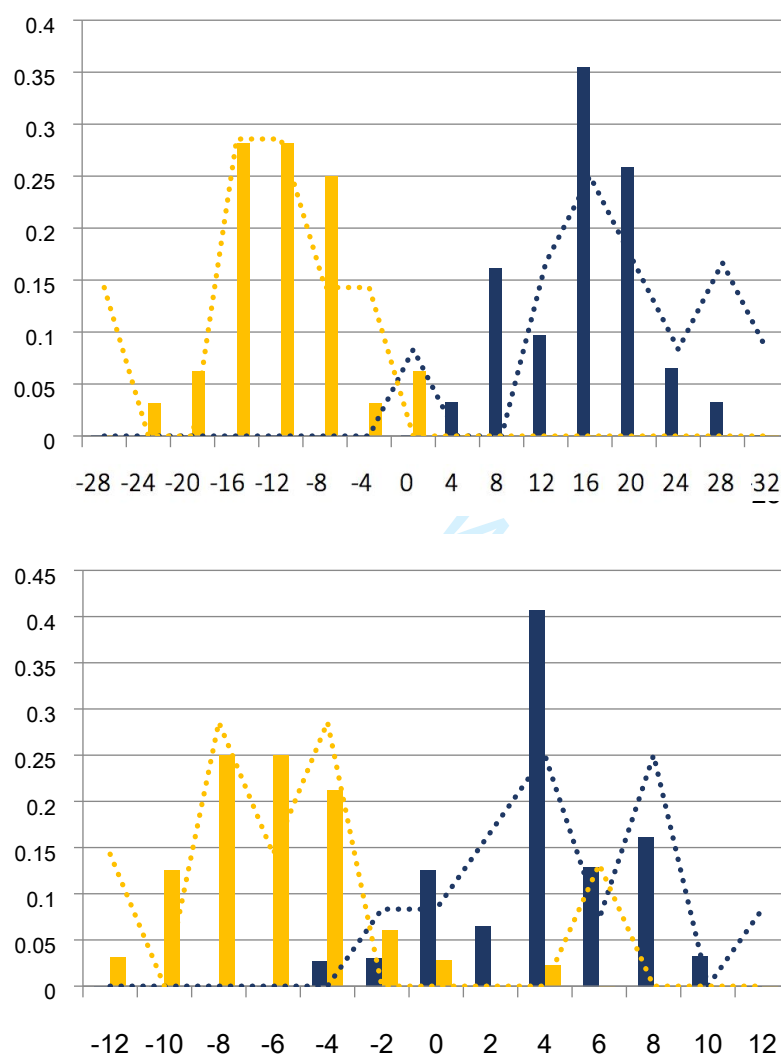
163 **Figure 1. PDDs for DF1 (top) and DF2 (bottom) used to determine activity intervals.**
164 *Yellow bars: active training, yellow dotted lines: active test, blue bars: inactive training, blue*
165 *dotted lines: inactive test.*

166

167 Compounds that only satisfied one or none of the DFs were considered inactive.

168 The model classified correctly all inactive compounds, both in the training and the test

169 sets. As for active compounds, 29 (93.5%) were correctly classified in the training set

170   and 11 (91.7%) in the test set. The total accuracy of the model was of 96.3% (Table 1)

171   **and the Matthew's correlation coefficient is 0.89.**

172   Table 1. Classification accuracy for combination of DF1 and DF2 for the prediction of
173   antibacterial activity against *E. coli*.

Group	Active	Inactive	Accuracy (%)
Training active	29	2	93.5
Training inactive	0	32	100
Test active	11	1	91.7
Test inactive	0	7	100
TOTAL	**40**	**20**	**96.3**

174

175   Regarding the indexes affecting the values of DF1, there is a positive sign

176   associated with the presence of ramifications ($^5\chi_p$), the electrotopological index for

177   hydrogen atoms bonded to sp^2 carbons (SH_{tCH}), and the presence of Cl atoms (S_{Cl}). On

178   the other hand, the order 0 valence connectivity index ($^0\chi_v$), directly associated with

179   molecular volume [22], the presence of methanetriyl groups ($S_{>CH-}$), and the valence

180   charge index $^4G^v$, directly related with the dipolar moment [23], have a negative effect

181   on the values of DF1.

182   It is worth noting that the presence of chlorine atoms in the molecule favors its

183   antibacterial activity. This was experimentally observed by Fouramadi *et al*. [24], who

184   proved that the potency of a molecule against *E. coli* increased by substituting hydrogen

185   with fluorine and was drastically superior if these were replaced with chlorine atoms

186   (Figure 2).

	MIC (μg/mL)
R = H	6,25
R = F	1,56
R = Cl	0,025

188   Figure 2. MIC of a quinolone against *E. coli* depending on the substituents.

189

190   Regarding the values of DF2, a positive correlation can be observed with the

191   quotient between valence and non-valence order 0 connectivity index (^0C). On the other

192   hand, this correlation is negative with the quotient between valence and non-valence

193   order 2 connectivity index (^2C). This indicates the importance of an appropriate polarity

194 of the molecule, to which these indexes are associated [20]. Similarly, the values of DF2

195 are negatively affected by valence order 4 cluster connectivity index ($^4\chi_C v$), directly

196 related to molecular volume [25], and the number of types of topologically equivalent

197 vertices (*Nclass*), which is associated to molecular size and complexity.

198 When analyzing the indices in both DFs, the presence of a discrete index was

199 detected in DF2, *Nclass*. It was observed that active compounds were grouped within a

200 certain range of values for this index. Following, the empirical distribution of the active

201 and inactive compounds depending on their value for *Nclass* was studied. Analyzing the

202 probability distribution of Figure 3, it was determined that the range of values in which

203 there is a higher probability of finding an active compound is when *Nclass* has values

204 between 11 and 16. This range includes 95.3% of the active compounds. In view of this

205 distribution, *Nclass* can be considered as a new SAR of the antibacterial quinolones

206 against *E. coli*.

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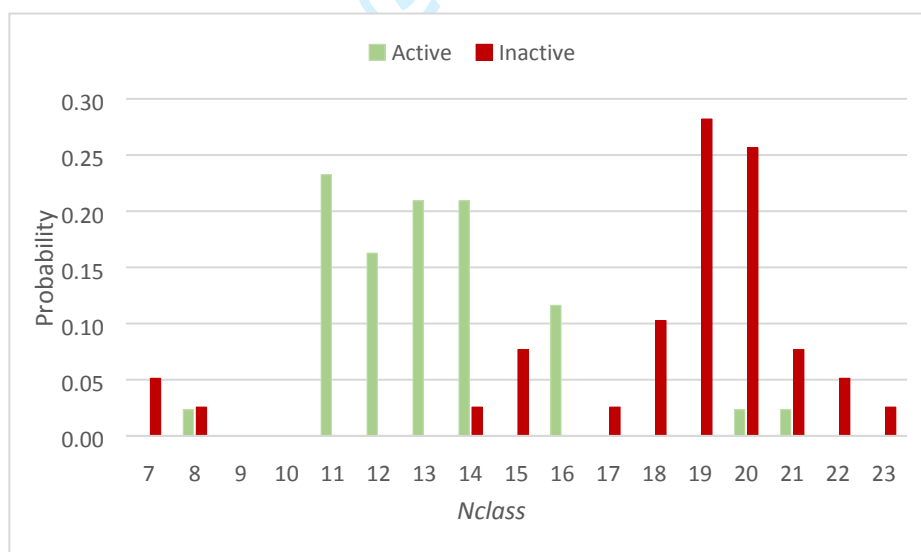
209 Figure 3. Probability distribution for active and inactive compounds according to their
210 *Nclass* values.

211

212 Regarding the provided definition for *Nclass,* number of classes of topologically

213 (symmetry) equivalent graph vertices [18], it must be noted that we could not find any

214 relationship between the term "symmetry" that appears in the definition and the values

215 of *Nclass* calculated for the molecules used to build the model. The only reference we

216 have found that discusses the nature of this index is an article by Stanton [26] in which

217   he defines *Nclass* as the number of classes of connectivity types identified in a structure.

218   He suggests that this index measures the size and complexity of the molecule, increasing

219   its value proportionally to these factors. Stanton explains that each type of topological

220   substructure (first-order path, second-order path, etc.) are each considered a separate

221   topological class.

222   Studying this index, we have concluded that, for practical purposes, it **should be**

223   **defined** as the topological distance (number of axis) between the two farthest vertices
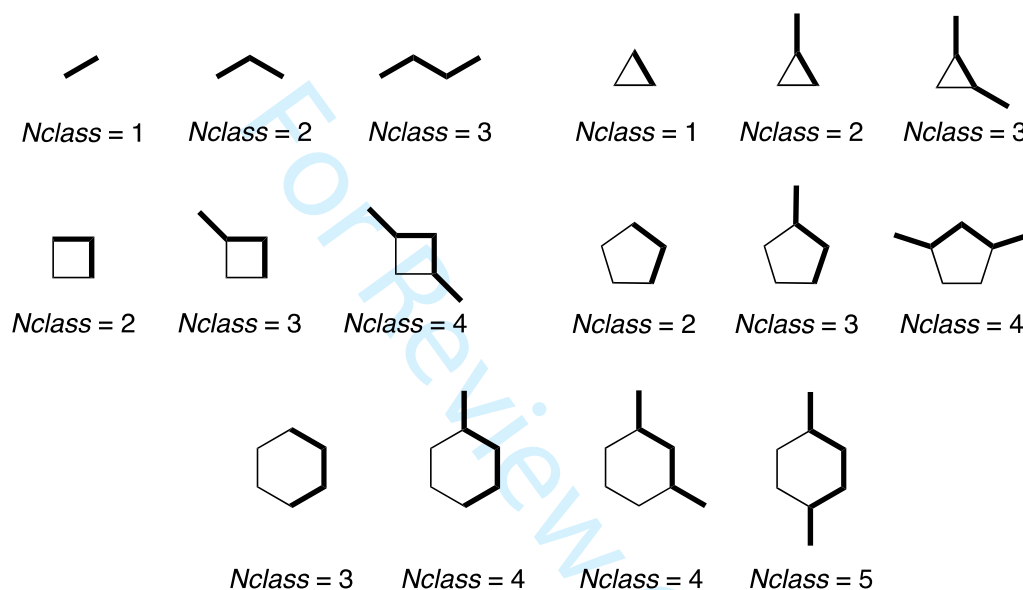
224   of a graph through the shortest path (Figure 4).

Nclass = 1   *Nclass* = 2   *Nclass* = 3   *Nclass* = 1   *Nclass* = 2   *Nclass* = 3

Nclass = 2   *Nclass* = 3   *Nclass* = 4   *Nclass* = 2   *Nclass* = 3   *Nclass* = 4

Nclass = 3   *Nclass* = 4   *Nclass* = 4   *Nclass* = 5

225

226   Figure 4. Examples of structures with different *Nclass* values.

227

228   Once both groups were defined, it was established that all compounds with

229   values for Nclass outside the 11-16 range would be directly considered inactive. As for

230   those with values within the range 11-16, DF1 would be applied to determine their

231   activity. Thus, in order for a compound to be classified as active it must have a value for

232   Nclass within 11-16 and a value for DF1 within 0-32. **As in the previous case, to avoid**

233   **false actives, compounds with values for DF1 > 32 are considered unclassifiable.**

234

235   As it can be observed in Table 2, this model appears to have a lower accuracy

236   percentage for active compounds, however, this is due to the fact that the model is more

237   restrictive, which also means that it will be more efficient in discarding inactive

238   compounds and, therefore, avoiding false actives. **Moreover, the discriminatory power**

239 **of the model remains unchanged, as shown by its Matthew's correlation coefficient,**

240 **0.89.**

241

242 Table 2. Classification accuracy for the Prediction Model of antibacterial activity against

243 *E. coli*.

Group	Active	Inactive	Accuracy (%)
Training active	20	11	64.5
Training inactive	0	32	100
Test active	11	1	91.7
Test inactive	0	7	100
TOTAL	**31**	**51**	**89.1**

244

245

246 *Model validation (Virtual screening)*

247 **Traditionally, the search of new active compounds using QSAR methods**

248 **consists in applying the model to the same family of compounds used for its**

249 **construction. This is obligatory when the model is obtained using fragmentary**

250 **parameters [27]. However, the use of overall connectivity parameters along with LDA**

251 **[28] allows its application to compounds with large structural diversity, yielding**

252 **excellent results [21, 29, 30].**

253 The model was used for the screening of the virtual library created using the

254 Index Merck database. The model selected 113 theoretically active compounds, of

255 which 47 (42%) had already been described as active against *E. coli* in bibliography. On

256 the other hand, when the combination of DF1 and DF2 is used as a model for the virtual

257 screening of Index Merck 174 molecules are selected as theoretically active but only

258 27% are described as active against *E. coli* in bibliography (the theoretically active

259 compounds and their values for the DFs and *Nclass* can be found in the Supporting

260 Information).

261 These results show that the model that combines DF1 and *Nclass* results more

262 restrictive and increases the success rate.

263

264 **CONCLUSIONS.**

265 The prediction model obtained highlights the importance of molecular size and

266 complexity, represented with *Nclass*, for the antibacterial activity of quinolones against

267   *E. coli*. In fact, the *Nclass* index could be included as a filter in existing prediction models

268   for antibacterial activity against *E. coli*. The results obtained prove that molecular

269   topology is a cost-effective, potent and useful tool for the discovery and selection of

270   new antibacterial compounds against *E. coli*.

271

272   **FUTURE PERSPECTIVES.**

273   Antibiotic resistance has rapidly become a global threat to the public health. The

274   increasing rate of antibiotic-resistant bacteria calls for the constant and urgent

275   introduction of new antibacterial treatments in the market. However, R&D from the

276   pharmaceutical industry in this field is scarce and continues to decrease. Therefore, any

277   breakthrough, however small, made in this field will be of great help to minimize this

278   problem. It is here where QSAR methods play a key role in the future of these

279   treatments. These methods allow the identification of theoretically active molecules in

280   a time- and cost-effective manner. Moreover, we currently live in the world of Big Data,

281   with a constantly growing number of databases containing thousands of chemical

282   compounds. The prediction model developed in this article could be applied to any of

283   these chemical databases in order to find new active compounds against *E. coli*.

284   Furthermore, the topological index *Nclass* can act as a filter in other QSAR models

285   predicting activity against *E. coli* in the same way that the Lipinski's Rule of 5 is used for

286   selecting drug-like molecules. The methodology used to develop this prediction model

287   could also be used to construct models against other resistant bacteria that pose a

288   threat to the public health. On the other hand, an exhaustive search for quinolones has

289   been carried out and structural and activity data are collected. These data can be used

290   by other groups to develop QSAR models with other methodologies. Overall, we

291   consider that QSAR prediction models will continue to evolve and be used for the

292   development of new antibacterial compounds in the fight against drug-resistant

293   bacteria.

294

295

296   **SUMMARY POINTS**

297   • Antibiotic resistance is a serious problem that affects worldwide

298   • There is a lack of research from the pharmaceutical industry

299 • The search and development of new antibiotics falls on universities and research

300 centers. QSAR methods appear as one of the most effective tools for this

301 purpose.

302 • A mathematical-topological model with good statistical parameters, capable of

303 selecting compounds with activity against *E. coli*, has been developed.

304 • The prediction model obtained highlights the importance of molecular size and

305 complexity, represented with *Nclass*, for the antibacterial activity of quinolones

306 against *E. coli*.

307 • The topological index *Nclass* could be considered as a new SAR of the

308 antibacterial quinolones against *E. coli*.

309 • The model has been applied to a database of more than 6000 compounds

310 selecting 113 compounds as theoretically active, of which 42% have proven

311 antibacterial activity against *E. coli*.

312 • The remaining 66 compounds are strong candidates to be developed as new

313 drugs against *E. coli.*

314 • Molecular topology is a cost-effective, potent and useful tool for the discovery

315 and selection of new antibacterial compounds against *E. coli.*

316

317 **SUPPLEMENTARY INFORMATION**

318 Supporting information contains definitions of the topological indexes used to obtain

319 the DFs, results for the LDA of the chosen DFs and the compounds selected by the model

320 as theoretically active. It also contains information regarding the quinolones used for

321 the construction of the DFs.

322

323 **FINANCIAL & COMPETING INTERESTS DISCOLSURE**

324 The authors have no relevant affiliations or financial involvement with any organization

325 or entity with financial interest in or financial conflict with the subject matter or

326 materials discussed in the manuscript. This includes employment, consultancies,

327 honoraria, stock ownership or options, expert testimony, grants or patents received or

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330

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SUPPORTING INFORMATION

Table S1. Symbols and definitions of the topological indexes used with DESMOL13[1] and MOLCONN-Z[2] programs.

Symbol	Name	Definition	Refs.
Connectivity indexes			
$^k\chi_t$ k=0-10 t=p,c,pc	Kier-Hall indexes Kier-Hall of order k y type path (p), cluster (c) and path-cluster (pc)	$$^k\chi_t = \sum_{j=1}^{^k n_t} \left(\prod_{i \in S_j} \delta_i \right)^{-1/2}$$ δ_i: number of bonds, σ or π of the atom i to non-hydrogen atoms. $S_{j,}$: jth substructure of order k and type t.	3
$^k\chi_t^{\,v}$ k=0-10 t=p,c,pc	Kier-Hall indexes of order k and type path (p), cluster (c) and path-cluster (pc)	$$^k\chi_t^{\,v} = \sum_{j=1}^{^k n_t} \left(\prod_{i \in S_j} \delta_i^{\,v} \right)^{-1/2}$$ $\delta_i^{\,v}$: Kier-Hall valence of the atom i. $S_{j,}$: jth substructure of order k and type t.	2
^kD_t k=0-4 t=p,c,pc	Connectivity differences of order k and type path (p), cluster (c) and path-cluster (pc)	$$^kD_t = {^k\chi_t} - {^k\chi_t^{\,v}}$$	2
^kC_t k=0-4 t=p,c,pc	Connectivity ratios of order k and type path (p), cluster (c) and path-cluster (pc)	$$^kC_t = {^k\chi_t} / {^k\chi_t^{\,v}}$$	2
Charge indexes			
G_k k=1-5	Topological charge index of order k	$$G_k = \sum_{i=1}^{N-1} \sum_{j=i+1}^{N} \left| \mathbf{M}_{ij} - \mathbf{M}_{ji} \right| \delta(k, \mathbf{D}_{ij})$$ **M=A.Q**: product of the adjacency and inverse squared distance matrixes for the hydrogen-depleted molecular graph. **D**: distance matriz. δ: Kronecker delta.	4
$G_k^{\,v}$ k=1-5	Valence topological charge index of order k	$$G_k^{\,v} = \sum_{i=1}^{N-1} \sum_{j=i+1}^{N} \left| \mathbf{M}_{ij}^{\,v} - \mathbf{M}_{ji}^{\,v} \right| \delta(k, \mathbf{D}_{ij})$$ **M^v=A^v.Q**: product of the electronegativity-modified adjacency and inverse squared distance matrixes for the hydrogen-depleted molecular graph. **D**: distance matrix. δ: Kronecker delta.	4
$J_k, J_k^{\,v}$ k=1-5	Pondered topological charge indexes of order k	$$J_k = \frac{G_k}{N-1} \qquad J_k^{\,v} = \frac{G_k^{\,v}}{N-1}$$	4

Electrotopological indexes			
$S^T(i)$	Sum of electrotopological indexes for a type of atom i	$S_i = I_i + \Delta I_i$ I_i: intrinsic state value of atom i. ΔI_i: delta value for the intrinsic topological state for the atom type i.	5
Gmaxpos	Gmaxpos index	Maximum positive value for the electrotopological state of non-hydrogen atoms in the molecule.	6
Hmaxpos	Hmaxpos index	Maximum positive value for the electrotopological state of hydrogen atoms in the molecule.	7
Molecular properties			
N	Molecular size	Number of non-hydrogen atoms.	4
L	Length	Maximum distance between atoms in terms of bonds	4
PR_i	PR0 to PR3	Number of pairs of ramifications separated by i atoms.	4
R	Ramification	Number of simple structural branches.	1
V_k $k=3,4$	Grade k vertexes	Number of atoms with k σ or π bonds, with other atoms (hydrogens not included).	4
knotp	Knotp index	Difference between $^3\chi_c$ and $^4\chi_{pc}$ indexes	8
knotpv	knotpv index	Difference between $^3\chi^v_c$ and $^4\chi^v_{pc}$ indexes	8
numhbd	Numhbd index	Number of hydrogen-donating atoms in a molecule.	8
numhba	Numhbd index	Number of hydrogen-accepting atoms in a molecule.	8
Information indexes			
$I_{Shannon}$	Shannon index	Index based on the atomic diversity of the molecule.	9
NI, NI2	NI, NI2 index	Indexes based on information theory.	9
BonIdW	Bonchev IdW(G) index	Index based on the distribution of topological distances in the molecule.	10
BonIdG	Bonchev Id(G) index	Index based on the numer of order 2 subgraphs in the molecule.	10
Molecular shape indexes			
$^n\kappa$ $n=1\text{-}3$	Kappa index of order n	$^1\kappa = N(N-1)^2/(^1P)^2$ $^2\kappa = (N-1)(N-2)^2/(^2P)^2$ $^3\kappa = (N-3)(N-2)^2/(^3P)^2$ [N even; N>3] $^3\kappa = (N-1)(N-3)^2/(^3P)^2$ [N odd; N>3] N: number of atoms (hydrogens not included) $^{1,2,3}P$: number of path type subgraphs of orders 1, 2 and 3.	11
$^n\kappa_\alpha$ $n=1\text{-}3$	Kappa-alpha index of order n	$^1\kappa = N+\alpha(N+\alpha-1)^2/(^1P+\alpha)^2$ $^2\kappa = (N+\alpha-1)(N+\alpha-2)^2/(^2P+\alpha)^2$ $^3\kappa = (N+\alpha-3)(N+\alpha-2)^2/(^3P+\alpha)^2$ [N even; N>3]	11

		$^3\kappa = (N+\alpha-1)(N+\alpha-3)^2/(^3P+\alpha)^2$ [N odd; N>3] N: number of non-hydrogen atoms. $^{1,2,3}P$: number of path type subgraphs of orders 1, 2 and 3. $\alpha = \Sigma[(R_i / R_{Csp3})-1]$ R_i: covalent radius for atom *i*. R_{Csp3}: covalent radius for atom *Csp³*.	
ϕ	Phia flexibility index	$\Phi = (^1\kappa \cdot {}^2\kappa) / N$ N: number of non-hydrogen atoms.	12
Global topological indexes			
Sum-I	Sum of the intrinsic state values	$I_i = \dfrac{\delta_i^v + 1}{\delta_i}$; $\text{Sum} - I = \sum I_i$ δ_i, number of σ or π bondsot the atom *i* con to other non-hydrogen atoms. δ_i^v, Kier-Hall valence of the atom *i*.	5
Sum-ΔI	Sum of the change in intrinsic state values	$\Delta I = \dfrac{I_i - I_j}{r_{ij}^2}$; $\text{Sum} - \Delta I = \sum \dfrac{I_i - I_j}{r_{ij}^2}$ r_{ij}, number of vertexes between *i* and *j* atoms.	5
TETS2	Total electrotopological state index	Sum of all the electrotopological indexes in the molecule.	8
TTd4	TTd4 index	Sum of the intrinsic states of all the atoms in the molecule.	8
nclass	Symmetry index	Number of symmetrically equivalent types of atoms.	13
W	Wiener index	Sum of the topological distances between all the non-hydrogen atoms by the shortest path.	14
Wp	Wiener polarity index	Number of pairs of atoms with a distance of 3 bonds.	15
Ww	Hyper-Wiener Index	Sum of the topological distances and the squared topological distances between all the non-hydrogen atoms by the shortest path.	15
Wt	Total Wiener index	Sum of the topological distances between all the non-hydrogen atoms by the longest path.	15
PlattF	PlattF index	Sum of the degrees of the bonds.	16

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Table S2. Structure and references on *E. coli* activity of the compounds used to develop the model.

Compound	IUPAC Name	Structure	References
Act1	(*E*)-7-(3-amino-4-(methoxyimino)piperidin-1-yl)-6-fluoro-1-(2-fluorocyclopropyl)-8-methoxy-4-oxo-1,4-dihydroquinoline-3-carboxylic acid		Liu H, Huang J, Wang J et al. Synthesis, antimycobacterial and antibacterial evaluation of I-[(1R, 2S)-2-fluorocyclopropyl]fluoroquinolone derivatives containing an oxime functional moiety. Eur J Med Chem 2014; 86:628-638.
Act2	(*E*)-7-(2-(aminomethyl)-3-(methoxyimino)azetidin-1-yl)-6-fluoro-1-(2-fluorocyclopropyl)-8-methoxy-4-oxo-1,4-dihydroquinoline-3-carboxylic acid		Idem
Act3	(*E*)-7-(3-amino-4-(methoxyimino)piperidin-1-yl)-6-fluoro-1-(2-fluorocyclopropyl)-4-oxo-1,4-dihydroquinoline-3-carboxylic acid		Idem
Act4	(*Z*)-7-(3-(aminomethyl)-4-(methoxyimino)pyrrolidin-1-yl)-6-fluoro-1-(2-fluorocyclopropyl)-4-oxo-1,4-dihydroquinoline-3-carboxylic acid		Idem
Act5	(*Z*)-7-(3-(aminomethyl)-4-(ethoxyimino)pyrrolidin-1-yl)-6-fluoro-1-(2-fluorocyclopropyl)-4-oxo-1,4-dihydroquinoline-3-carboxylic acid		Idem
Act6	(*Z*)-7-(3-(aminomethyl)-4-(phenoxyimino)pyrrolidin-1-yl)-6-fluoro-1-(2-fluorocyclopropyl)-4-oxo-1,4-dihydroquinoline-3-carboxylic acid		Idem

Act7	(*E*)-7-(2-(aminomethyl)-3-(methoxyimino)azetidin-1-yl)-6-fluoro-1-(2-fluorocyclopropyl)-4-oxo-1,4-dihydroquinoline-3-carboxylic acid		Idem
Act8	(*E*)-7-(2-(aminomethyl)-3-(ethoxyimino)azetidin-1-yl)-6-fluoro-1-(2-fluorocyclopropyl)-4-oxo-1,4-dihydroquinoline-3-carboxylic acid		Idem
Act9	(*E*)-7-(2-(aminomethyl)-3-(phenoxyimino)azetidin-1-yl)-6-fluoro-1-(2-fluorocyclopropyl)-4-oxo-1,4-dihydroquinoline-3-carboxylic acid		Idem
Act13	(*Z*)-7-(3-(aminomethyl)-4-(methoxyimino)pyrrolidin-1-yl)-8-chloro-6-fluoro-1-(2-fluorocyclopropyl)-4-oxo-1,4-dihydroquinoline-3-carboxylic acid		Idem
Act14	(*Z*)-7-(3-(aminomethyl)-4-(ethoxyimino)pyrrolidin-1-yl)-8-chloro-6-fluoro-1-(2-fluorocyclopropyl)-4-oxo-1,4-dihydroquinoline-3-carboxylic acid		Idem
Act15	(*Z*)-7-(3-(aminomethyl)-4-(phenoxyimino)pyrrolidin-1-yl)-8-chloro-6-fluoro-1-(2-fluorocyclopropyl)-4-oxo-1,4-dihydroquinoline-3-carboxylic acid		Idem
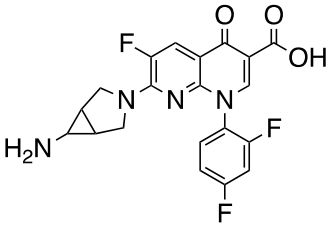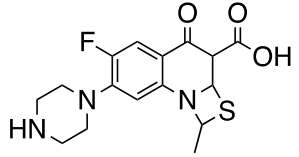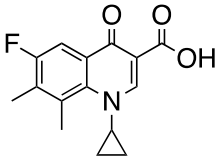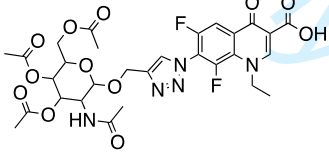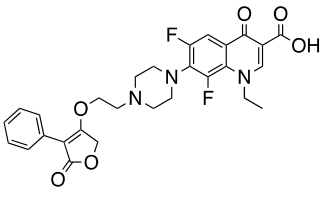
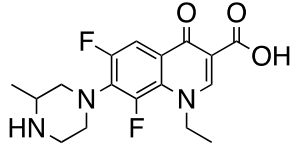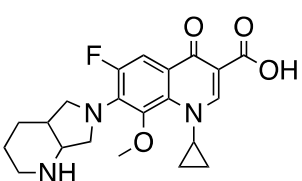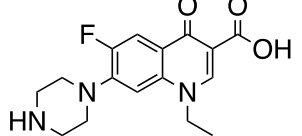|			
Act16	(*E*)-7-(3-amino-4-(methoxyimino)piperidin-1-yl)-6-fluoro-1-(2-fluorocyclopropyl)-4-oxo-1,4-dihydro-1,8-naphthyridine-3-carboxylic acid		Idem
Act17	(*Z*)-7-(3-(aminomethyl)-4-(methoxyimino)pyrrolidin-1-yl)-6-fluoro-1-(2-fluorocyclopropyl)-4-oxo-1,4-dihydro-1,8-naphthyridine-3-carboxylic acid		Idem
Act18	(*Z*)-7-(3-(aminomethyl)-4-(ethoxyimino)pyrrolidin-1-yl)-6-fluoro-1-(2-fluorocyclopropyl)-4-oxo-1,4-dihydro-1,8-naphthyridine-3-carboxylic acid		Idem
Act19	(*Z*)-7-(3-(aminomethyl)-4-(phenoxyimino)pyrrolidin-1-yl)-6-fluoro-1-(2-fluorocyclopropyl)-4-oxo-1,4-dihydro-1,8-naphthyridine-3-carboxylic acid		Idem
Act20	(*E*)-7-(2-(aminomethyl)-3-(methoxyimino)azetidin-1-yl)-6-fluoro-1-(2-fluorocyclopropyl)-4-oxo-1,4-dihydro-1,8-naphthyridine-3-carboxylic acid		Idem
Act21	(*E*)-7-(2-(aminomethyl)-3-(ethoxyimino)azetidin-1-yl)-6-fluoro-1-(2-fluorocyclopropyl)-4-oxo-1,4-dihydro-1,8-naphthyridine-3-carboxylic acid		Idem
Act22	(*E*)-7-(2-(aminomethyl)-3-(phenoxyimino)azetidin-1-yl)-6-fluoro-1-(2-fluorocyclopropyl)-4-oxo-1,4-dihydro-1,8-		Idem

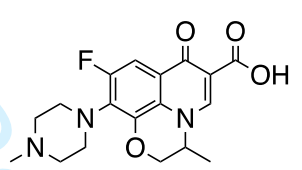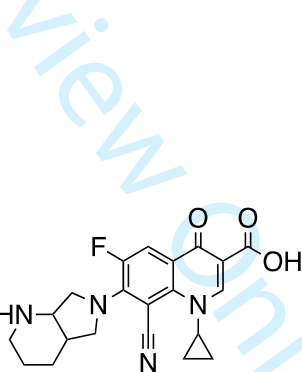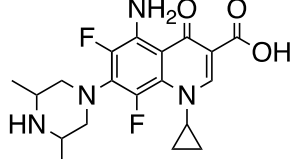|			
	naphthyridine-3-carboxylic acid		
Act26	6,8-difluoro-1-(4-fluorophenyl)-7-(4-(2-((4-(2-fluorophenyl)-5-oxo-2,5-dihydrofuran-3-yl)oxy)ethyl)piperazin-1-yl)-4-oxo-1,4-dihydroquinoline-3-carboxylic acid		Wang XD, Wei W, Wang PF et al. Novel 3-arylfuran-2(5H)-one-fluoroquinolone hybrid: design, synthesis and evaluation as antibacterial agent. Bioorg Med Chem 2014, 22(14):3620-3628.
Act27	1-cyclopropyl-6,8-difluoro-7-(4-(2-((4-(2-fluorophenyl)-5-oxo-2,5-dihydrofuran-3-yl)oxy)ethyl)piperazin-1-yl)-4-oxo-1,4-dihydroquinoline-3-carboxylic acid		Wang XD, Wei W, Wang PF et al. Novel 3-arylfuran-2(5H)-one-fluoroquinolone hybrid: design, synthesis and evaluation as antibacterial agent. Bioorg Med Chem 2014, 22(14):3620-3628.
Act32	(Z)-7-(3-(aminomethyl)-4-(methoxyimino)-3-methylpiperidin-1-yl)-1-cyclopropyl-6,8-difluoro-4-oxo-1,4-dihydroquinoline-3-carboxylic acid		Chai Y, Liu M, Wang B, et al. Synthesis and in vitro antibacterial activity of novel fluoroquinolone derivatives containing substituted piperidines. Bioorg Med Chem Lett 2010; 20(17):5195-5198.
Besifloxacin	7-(3-aminoazepan-1-yl)-8-chloro-1-cyclopropyl-6-fluoro-4-oxo-1,4-dihydroquinoline-3-carboxylic acid		CLSI Performance Standards for Antimicrobial Susceptibility Testing, 26th Edition.
Ciprofloxacin	1-cyclopropyl-6-fluoro-4-oxo-7-(piperazin-1-yl)-1,4-dihydroquinoline-3-carboxylic acid		Idem
Clinafloxacino	7-(3-aminopyrrolidin-1-yl)-8-chloro-1-cyclopropyl-6-fluoro-4-oxo-1,4-dihydroquinoline-3-carboxylic acid		Idem
Delafloxacin	1-(6-amino-3,5-difluoropyridin-2-yl)-8-chloro-6-fluoro-7-(3-hydroxyazetidin-1-yl)-4-oxo-1,4-dihydroquinoline-3-carboxylic acid		Idem

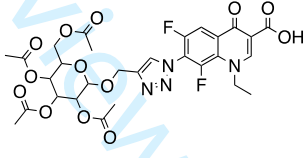|			
Enoxacin	1-ethyl-6-fluoro-4-oxo-7-(piperazin-1-yl)-1,4-dihydro-1,8-naphthyridine-3-carboxylic acid		Idem
Finafloxacin	8-cyano-1-cyclopropyl-6-fluoro-7-(hexahydropyrrolo[3,4-b][1,4]oxazin-6(2H)-yl)-4-oxo-1,4-dihydroquinoline-3-carboxylic acid		Idem
Fleroxacin	6,8-difluoro-1-(2-fluoroethyl)-7-(4-methylpiperazin-1-yl)-4-oxo-1,4-dihydroquinoline-3-carboxylic acid		Idem
Garenoxacin	1-cyclopropyl-8-(difluoromethoxy)-6-fluoro-7-(1-methylisoindolin-5-yl)-4-oxo-1,4-dihydroquinoline-3-carboxylic acid		Idem
Gatifloxacin	1-cyclopropyl-6-fluoro-8-methoxy-7-(3-methylpiperazin-1-yl)-4-oxo-1,4-dihydroquinoline-3-carboxylic acid		Idem
Gemifloxacin	(Z)-7-(3-(aminomethyl)-4-(methoxyimino)pyrrolidin-1-yl)-1-cyclopropyl-6-fluoro-4-oxo-1,4-dihydro-1,8-naphthyridine-3-carboxylic acid		Idem
Grepafloxacin	1-cyclopropyl-6-fluoro-5-methyl-7-(3-methylpiperazin-1-yl)-4-oxo-1,4-dihydroquinoline-3-carboxylic acid		Idem
Levofloxacin	9-fluoro-3-methyl-10-(4-methylpiperazin-1-yl)-7-oxo-2,3-dihydro-7H-[1,4]oxazino[2,3,4-ij]quinoline-6-carboxylic acid		Idem

	1-ethyl-6,8-difluoro-7-(3-methylpiperazin-1-yl)-4-oxo-1,4-dihydroquinoline-3-carboxylic acid		Idem
Lomefloxacin			Idem
Moxifloxacin	1-cyclopropyl-6-fluoro-8-methoxy-7-(octahydro-6*H*-pyrrolo[3,4-*b*]pyridin-6-yl)-4-oxo-1,4-dihydroquinoline-3-carboxylic acid		Idem
Norfloxacin	1-ethyl-6-fluoro-4-oxo-7-(piperazin-1-yl)-1,4-dihydroquinoline-3-carboxylic acid		Idem
Ofloxacin	9-fluoro-3-methyl-10-(4-methylpiperazin-1-yl)-7-oxo-2,3-dihydro-7*H*-[1,4]oxazino[2,3,4-*ij*]quinoline-6-carboxylic acid		Idem
Pradofloxacin	8-cyano-1-cyclopropyl-6-fluoro-7-(octahydro-6*H*-pyrrolo[3,4-*b*]pyridin-6-yl)-4-oxo-1,4-dihydroquinoline-3-carboxylic acid		Pridmore A, Stephan B, Griefe HA. In vitro activity of pradofloxacin against clinical isolates from European field studies In: Proceedings of the American Society for Microbiology (ASM) 105th General Meeting, Atlanta, GA, USA p617, 2005. Abraham J, Ewet K, de Jong A. Pradofloxacin: Comparative in vitro activity against selected pathogens from the US. In: 42nd Interscience Conference on Antimicrobial Agents and Chemotherapy, San Diego, CA, USA p.189.
Sparfloxacin	5-amino-1-cyclopropyl-7-(3,5-dimethylpiperazin-1-yl)-6,8-difluoro-4-oxo-1,4-dihydroquinoline-3-carboxylic acid		Idem

Trovafloxacin	7-(6-amino-3-azabicyclo[3.1.0]hexan-3-yl)-1-(2,4-difluorophenyl)-6-fluoro-4-oxo-1,4-dihydro-1,8-naphthyridine-3-carboxylic acid		Idem
Ulifloxacin	6-fluoro-1-methyl-4-oxo-7-(piperazin-1-yl)-2a,3-dihydro-1*H*,4*H*-[1,3]thiazeto[3,2-*a*]quinoline-3-carboxylic acid		Idem
PGE-8367769	1-cyclopropyl-6-fluoro-7,8-dimethyl-4-oxo-1,4-dihydroquinoline-3-carboxylic acid		Macinga DR, Renick PJ, Makin KM, et al. Unique biological properties and molecular mechanism of 5,6-bridged quinolones. Antimicrob Agents Chemother. 2003; 47(8):2526-2537.
Inact1	1-ethyl-6,8-difluoro-4-oxo-7-(4-(((3,4,5-triacetoxy-6-(acetoxymethyl)tetrahydro-2*H*-pyran-2-yl)oxy)methyl)-1*H*-1,2,3-triazol-1-yl)-1,4-dihydroquinoline-3-carboxylic acid		Azad CS, Bhunia SS, Krishna A, Shukla PK, Saxena AK. Novel Glycoconjugate of 8-Fluoro Norfloxacin Derivatives as Gentamicin-resistant Staphylococcus aureus Inhibitors: Synthesis and Molecular Modelling Studies. Chem Biol Drug Des. 2015; 86(4):440-446.
Inact2	7-(4-(((3-acetamido-4,5-diacetoxy-6-(acetoxymethyl)tetrahydro-2*H*-pyran-2-yl)oxy)methyl)-1*H*-1,2,3-triazol-1-yl)-1-ethyl-6,8-difluoro-4-oxo-1,4-dihydroquinoline-3-carboxylic acid		Idem
Inact3	1-ethyl-6,8-difluoro-4-oxo-7-(4-(2-((5-oxo-4-phenyl-2,5-dihydrofuran-3-yl)oxy)ethyl)piperazin-1-yl)-1,4-dihydroquinoline-3-carboxylic acid		Wang XD, Wei W, Wang PF et al. Novel 3-arylfuran-2(5H)-one-fluoroquinolone hybrid: design, synthesis and evaluation as antibacterial agent. Bioorg Med Chem. 2014, 22(14):3620-3628.

Inact4	7-(4-(2-((4-(4-chlorophenyl)-5-oxo-2,5-dihydrofuran-3-yl)oxy)ethyl)piperazin-1-yl)-1-ethyl-6,8-difluoro-4-oxo-1,4-dihydroquinoline-3-carboxylic acid		Idem
Inact5	1-cyclopropyl-6,8-difluoro-7-(4-(2-((4-(4-methoxyphenyl)-5-oxo-2,5-dihydrofuran-3-yl)oxy)ethyl)piperazin-1-yl)-4-oxo-1,4-dihydroquinoline-3-carboxylic acid		Idem
Inact6	1-cyclopropyl-6-fluoro-7-(4-(2-(4-methylpiperazin-1-yl)acetyl)piperazin-1-yl)-4-oxo-1,4-dihydroquinoline-3-carboxylic acid		Suresh N, Nagesh HN, Renuka J, et al. Synthesis and evaluation of 1-cyclopropyl-6-fluoro-1,4-dihydro-4-oxo-7-(4-(2-(4-substitutedpiperazin-1-yl)acetyl)piperazin-1-yl)quinoline-3-carboxylic acid derivatices as anti-tubercular and antibacterial agents. Eur J Med. 2014; 71:324-332.
Inact7	1-cyclopropyl-7-(4-(2-(4-(3,4-difluorophenyl)piperazin-1-yl)acetyl)piperazin-1-yl)-6-fluoro-4-oxo-1,4-dihydroquinoline-3-carboxylic acid		Idem
Inact8	7-(4-(2-(4-(bis(4-fluorophenyl)methyl)piperazin-1-yl)acetyl)piperazin-1-yl)-1-cyclopropyl-6-fluoro-4-oxo-1,4-dihydroquinoline-3-carboxylic acid		Idem
Inact9	1-ethyl-6-fluoro-7-(4-(5-(2-nitrophenyl)-1,3,4-thiadiazol-2-yl)piperazin-1-yl)-4-oxo-1,4-dihydroquinoline-3-carboxylic acid		Foroumadi A, Soltani F, Moshafi MH, Ashraf-Askari R. Synthesis and in vitro antibacterial activity of some N-(5-aryl-1,3,4-thiadiazole-2-yl)piperazinyl quinolone derivatives. Farmaco. 2003; 58(10):1023-1028.
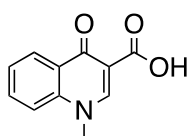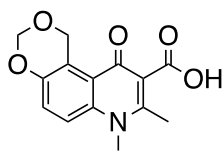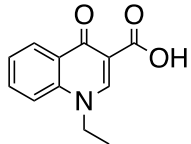
Inact10	1-ethyl-6-fluoro-7-(4-(5-(2-nitrophenyl)-1,3,4-thiadiazol-2-yl)piperazin-1-yl)-4-oxo-1,4-dihydro-1,8-naphthyridine-3-carboxylic acid		Idem
Inact11	1-cyclopropyl-6-fluoro-7-(4-(5-(3-nitrophenyl)-1,3,4-thiadiazol-2-yl)piperazin-1-yl)-4-oxo-1,4-dihydroquinoline-3-carboxylic acid		Idem
Inact12	1-ethyl-6-fluoro-7-(4-(5-(3-nitrophenyl)-1,3,4-thiadiazol-2-yl)piperazin-1-yl)-4-oxo-1,4-dihydroquinoline-3-carboxylic acid		Idem
Inact13	1-ethyl-6-fluoro-7-(4-(5-(3-nitrophenyl)-1,3,4-thiadiazol-2-yl)piperazin-1-yl)-4-oxo-1,4-dihydro-1,8-naphthyridine-3-carboxylic acid		Idem
Inact14	1-cyclopropyl-6-fluoro-7-(4-(5-(4-nitrophenyl)-1,3,4-thiadiazol-2-yl)piperazin-1-yl)-4-oxo-1,4-dihydroquinoline-3-carboxylic acid		Idem
Inact15	1-ethyl-6-fluoro-7-(4-(5-(4-nitrophenyl)-1,3,4-thiadiazol-2-yl)piperazin-1-yl)-4-oxo-1,4-dihydroquinoline-3-carboxylic acid		Idem
Inact16	1-ethyl-6-fluoro-7-(4-(5-(4-nitrophenyl)-1,3,4-thiadiazol-2-yl)piperazin-1-yl)-4-oxo-1,4-dihydro-1,8-naphthyridine-3-carboxylic acid		Idem

	1-cyclopropyl-6-fluoro-7-(4-(2-((6-nitrobenzo[*d*]thiazol-2-yl)amino)-2-oxoethyl)piperazin-1-yl)-4-oxo-1,4-dihydroquinoline-3-carboxylic acid		Sharma PC, Kumar R, Chaudhary M, Sharma A, Rajak H. Synthesis and biological evaluation of novel benzothiazole clubbed fluoroquinolone derivatives. J Enzyme Inhib Med Chem. 2013; 28(1):1-10.
Inact17			
Inact18	1-cyclopropyl-6-fluoro-7-(4-(2-((6-methylbenzo[*d*]thiazol-2-yl)amino)-2-oxoethyl)piperazin-1-yl)-4-oxo-1,4-dihydroquinoline-3-carboxylic acid		Idem
Inact19	1-cyclopropyl-6-fluoro-7-(4-(2-((6-fluorobenzo[*d*]thiazol-2-yl)amino)-2-oxoethyl)piperazin-1-yl)-4-oxo-1,4-dihydroquinoline-3-carboxylic acid		Idem
Inact20	7-(4-(2-((6-chlorobenzo[*d*]thiazol-2-yl)amino)-2-oxoethyl)piperazin-1-yl)-1-ethyl-6-fluoro-4-oxo-1,4-dihydroquinoline-3-carboxylic acid		Idem
Inact21	7-(4-(2-((5,7-dichlorobenzo[*d*]thiazol-2-yl)amino)-2-oxoethyl)piperazin-1-yl)-1-ethyl-6-fluoro-4-oxo-1,4-dihydroquinoline-3-carboxylic acid		Idem
Inact22	1-ethyl-6-fluoro-7-(4-(2-((6-nitrobenzo[*d*]thiazol-2-yl)amino)-2-oxoethyl)piperazin-1-yl)-4-oxo-1,4-dihydroquinoline-3-carboxylic acid		Idem
Inact23	1-ethyl-6-fluoro-7-(4-(2-((4-methylbenzo[*d*]thiazol-2-yl)amino)-2-oxoethyl)piperazin-1-yl)-4-oxo-1,4-		Idem

	dihydroquinoline-3-carboxylic acid		
Inact24	1-ethyl-6-fluoro-7-(4-(2-((4-fluorobenzo[*d*]thiazol-2-yl)amino)-2-oxoethyl)piperazin-1-yl)-4-oxo-1,4-dihydroquinoline-3-carboxylic acid		Idem
Inact25	7-(4-(2-((4-chlorobenzo[*d*]thiazol-2-yl)amino)-2-oxoethyl)-3-methylpiperazin-1-yl)-1-cyclopropyl-6-fluoro-8-methoxy-4-oxo-1,4-dihydroquinoline-3-carboxylic acid		Idem
Inact26	1-cyclopropyl-7-(4-(2-((6,7-dichlorobenzo[*d*]thiazol-2-yl)amino)-2-oxoethyl)-3-methylpiperazin-1-yl)-6-fluoro-8-methoxy-4-oxo-1,4-dihydroquinoline-3-carboxylic acid		Idem
Inact27	1-cyclopropyl-6-fluoro-8-methoxy-7-(3-methyl-4-(2-((4-nitrobenzo[*d*]thiazol-2-yl)amino)-2-oxoethyl)piperazin-1-yl)-4-oxo-1,4-dihydroquinoline-3-carboxylic acid		Idem
Inact28	1-cyclopropyl-6-fluoro-8-methoxy-7-(3-methyl-4-(2-((4-methylbenzo[*d*]thiazol-2-yl)amino)-2-oxoethyl)piperazin-1-yl)-4-oxo-1,4-dihydroquinoline-3-carboxylic acid		Idem
Inact29	1-cyclopropyl-6-fluoro-7-(4-(2-((4-fluorobenzo[*d*]thiazol-2-yl)amino)-2-oxoethyl)-3-methylpiperazin-1-yl)-		Idem

	8-methoxy-4-oxo-1,4-dihydroquinoline-3-carboxylic acid		
Inact30	(*Z*)-7-(3-(aminomethyl)-4-(ethoxyimino)-3-methylpiperidin-1-yl)-1-ethyl-6,8-difluoro-4-oxo-1,4-dihydroquinoline-3-carboxylic acid		Chai Y, Liu M, Wang B, et al. Synthesis and in vitro antibacterial activity of novel fluoroquinolone derivatives containing substituted piperidines. Bioorg Med Chem Lett. 2010; 20(17):5195-5198.
Inact31	(*Z*)-7-(3-(aminomethyl)-4-(ethoxyimino)-3-methylpiperidin-1-yl)-6,8-difluoro-1-(2-fluoroethyl)-4-oxo-1,4-dihydroquinoline-3-carboxylic acid		Idem
Inact32	(*Z*)-7-(3-(aminomethyl)-4-(ethoxyimino)-3-methylpiperidin-1-yl)-1-cyclopropyl-6-fluoro-8-methoxy-4-oxo-1,4-dihydroquinoline-3-carboxylic acid		Idem
Inact33	7-(4-cyclopentylpiperazin-1-yl)-1-ethyl-6-fluoro-4-oxo-1,4-dihydroquinoline-3-carboxylic acid		Abuo-Rahma Gel-D, Sarhan HA, Gad GF. Design, synthesis, antibacterial activity and physicochemical parameters of novel N-4-piperazinyl derivatives of norfloxacin. Bioorg Med Chem. 2009; 17(11):3879-3886.
Inact34	7-(4-(5,6-diphenyl-1,2,4-triazin-3-yl)piperazin-1-yl)-1-ethyl-6-fluoro-4-oxo-1,4-dihydroquinoline-3-carboxylic acid		Idem
Inact35	7-(4-((dimorpholinoamino)methyl)piperazin-1-yl)-1-ethyl-6-fluoro-4-oxo-1,4-dihydroquinoline-3-carboxylic acid		Idem
Inact36	7-(4-((bis(1,3-dioxoisoindolin-2-yl)amino)methyl)piperazin-1-yl)-1-ethyl-6-fluoro-4-oxo-1,4-		Idem

	dihydroquinoline-3-carboxylic acid		
PGE-5215205	1-methyl-4-oxo-1,4-dihydroquinoline-3-carboxylic acid		Macinga DR, Renick PJ, Makin KM, et al. Unique biological properties and molecular mechanism of 5,6-bridged quinolones. Antimicrob Agents Chemother. 2003; 47(8):2526-2537.
PGE-6116532	7,8-dimethyl-10-oxo-7,10-dihydro-1*H*-[1,3]dioxino[5,4-*f*]quinoline-9-carboxylic acid		Idem
PGE-9604297	1-ethyl-4-oxo-1,4-dihydroquinoline-3-carboxylic acid		Idem

Table S3. LDA results and classification of the compounds for DF1.

Compound	$^5\chi^p$	$^0\chi^v$	SH_{tCH}	$S_{>CH-}$	S_{Cl}	$^4G^v$	DF1	Prob.	Mahalanobis	Clas.
Act2	8.159	16.263	15.196	-2.304	0	5.023	16.321	1.000	3.3	+
Act3	7.579	15.639	14.907	-2.153	0	3.751	17.658	1.000	2	+
Act5	7.651	16.347	15.006	-1.819	0	4.097	10.166	1.000	1.9	+
Act6	8.833	18.026	15.205	-1.914	0	4.352	11.989	1.000	2.7	+
Act8	7.464	15.639	14.894	-2.074	0	3.877	14.862	1.000	1.2	+
Act9	8.649	17.319	15.093	-2.169	0	4.133	16.726	1.000	3.0	+
Act13	7.779	16.696	15.116	-2.037	6.558	4.406	15.117	1.000	5.9	+
Act15	9.120	19.083	15.381	-2.131	6.654	4.773	12.766	1.000	5.8	+
Act16	7.579	15.509	14.845	-2.296	0	3.992	16.902	1.000	1.3	+
Act17	7.492	15.509	14.877	-1.962	0	4.172	14.016	1.000	0.7	+
Act19	8.833	17.896	15.142	-2.056	0	4.539	11.575	1.000	1.8	+
Act20	7.299	14.802	14.766	-2.239	0	3.855	19.311	1.000	2.0	+
Act21	7.464	15.509	14.832	-2.239	0	3.966	15.132	1.000	1.1	+
Act22	8.649	17.189	15.031	-2.334	0	4.222	16.996	1.000	2.7	+
Act26	12.371	23.565	16.194	0	0	5.890	6.631	0.999	16.9	+
Act32	8.121	17.322	15.802	-0.120	0	5.229	6.501	0.999	5.5	+
Besifloxacin	7.123	15.507	15.023	0.007	6.633	3.933	12.765	1.000	5.4	+
Clinafloxacin	6.532	14.092	14.758	0.032	6.526	3.613	16.058	1.000	5.5	+
Delafloxacin	8.007	15.621	14.759	-0.705	6.358	3.525	24.452	1.000	10.8	+
Enoxacin	6.099	12.674	14.432	0	0	3.612	12.801	1.000	1.5	+

Fleroxacin	6.833	14.137	15.183	0	0	4.370	15.105	1.000	2.7	+
Gatifloxacin	7.517	15.289	15.102	0.291	0	4.947	7.809	1.000	4.3	+
Gemifloxacin	7.216	15.261	14.875	-0.023	0	4.177	6.489	0.998	3.0	+
Grepafloxacin	6.875	14.881	15.147	0.426	0	4.671	4.865	0.992	6.8	+
Lomefloxacin	6.625	13.975	15.193	0.075	0	4.215	14.678	1.000	2.7	+
Norfloxacin	6.099	12.804	14.495	0	0	3.492	13.239	1.000	1.4	+
Ofloxacin	7.953	14.659	14.984	-0.158	0	4.715	20.874	1.000	6.1	+
Pradofloxacin	8.563	15.819	15.249	0.709	0	4.714	19.388	1.000	5.3	+
Sparfloxacin	7.493	15.629	15.645	-0.104	0	4.874	13.855	1.000	3.9	+
Ulifloxacin	6.959	13.976	14.618	-1.466	0	3.326	21.277	1.000	3.1	+
PGE-8367769	5.496	10.174	12.289	0	0	2.886	1.606	0.833	21.3	+
Inact1	12.108	26.131	15.833	-7.289	0	7.440	-13.655	1.000	23.2	-
Inact2	12.108	16.223	15.841	-6.715	0	7.409	-15.991	1.000	19.8	-
Inact3	10.359	21.284	15.689	0	0	6.169	-8.384	1.000	2.2	-
Inact4	10.595	22.341	15.704	0	5.942	6.347	-10.479	1.000	4.6	-
Inact5	11.041	22.899	15.925	-0.128	0	6.454	-12.327	1.000	2.2	-
Inact6	8.869	19.374	15.133	0.128	0	5.743	-16.446	1.000	1.8	-
Inact7	10.807	22.362	14.258	0.086	0	6.582	-21.603	1.000	2.6	-
Inact10	10.006	20.313	15.078	0	0	6.222	-13.239	1.000	0.6	-
Inact12	9.864	20.443	15.134	0	0	6.046	-14.485	1.000	0.2	-
Inact13	9.864	20.313	15.072	0	0	6.166	-14.923	1.000	0.4	-
Inact14	9.999	20.728	15.242	0.105	0	6.027	-13.978	1.000	0.4	-
Inact15	9.661	20.443	15.129	0	0	6.100	-17.686	1.000	0.9	-
Inact16	9.661	20.313	15.066	0	0	6.220	-18.124	1.000	1.2	-
Inact17	10.579	21.818	15.214	0.084	0	5.569	-13.815	1.000	5.2	-
Inact19	10.249	20.933	15.184	0.097	0	5.489	-9.911	1.000	4.0	-
Inact20	9.911	21.404	15.086	0	6.018	5.596	-15.126	1.000	4.8	-
Inact21	10.076	22.461	15.105	0	12.24	5.869	-18.458	1.000	20.0	-
Inact22	10.241	21.534	15.101	0	0	5.642	-17.589	1.000	3.9	-
Inact23	9.874	21.270	15.098	0	0	5.999	-22.417	1.000	3.9	-
Inact25	11.449	23.889	15.606	-0.094	6.208	7.119	-17.936	1.000	5.8	-
Inact27	11.951	24.019	15.713	-0.194	0	7.173	-17.932	1.000	2.1	-
Inact28	11.449	23.756	15.705	-0.066	0	7.494	-24.839	1.000	5.5	-
Inact29	11.449	23.134	15.678	-0.147	0	7.022	-16.101	1.000	1.3	-
Inact30	7.887	17.744	15.655	0	0	5.413	-4.360	0.987	8.6	-
Inact31	8.027	17.829	15.669	0	0	5.408	-3.019	0.953	8.8	-
Inact32	8.783	19.059	15.565	0.041	0	6.145	-10.641	1.000	4.5	-
Inact33	7.254	16.157	14.899	0.669	0	3.813	-0.949	0.721	12.6	-

Inact34	11.763	22.366	15.333	0	0	7.261	-11.529	1.000	6.1	-
Inact35	10.137	21.273	15.249	0	0	6.101	-17.285	1.000	1.0	-
Inact36	14.238	25.051	15.478	0	0	8.708	-10.164	1.000	27.6	-
PGE-6116542	5.534	11.096	12.509	0	0	3.868	-9.599	1.000	16.7	-
PGE-9604297	3.866	8.805	11.844	0	0	2.026	-8.748	1.000	21.9	-
Act1	8.447	16.970	15.275	-2.358	0	5.128	14.206	1.000	2.8	+
Act4	7.492	15.639	14.939	-1.819	0	3.986	14.431	1.000	0.8	+
Act7	7.299	14.932	14.828	-2.075	0	3.766	19.042	1.000	1.7	+
Act14	7.938	17.403	15.182	-2.036	6.584	4.518	10.876	1.000	6.3	+
Act18	7.651	16.216	14.943	-1.961	0	4.283	9.750	1.000	1.6	+
Act27	11.059	21.869	15.892	-0.143	0	6.153	-0.862	0.297	11.0	-
Ciprofloxacin	6.438	13.088	14.608	0.188	0	3.419	16.691	1.000	1.5	+
Finafloxacin	8.563	15.521	15.208	-0.038	0	4.689	24.096	1.000	8.4	+
Garenoxacin	9.017	16.993	15.369	-3.330	0	4.279	31.564	1.000	16.2	+
Levofloxacin	7.953	14.659	14.984	-0.158	0	4.715	20.874	1.000	6.1	+
Moxifloxacin	8.563	16.281	15.320	0.887	0	4.973	13.866	1.000	3.5	+
Trovafloxacin	8.393	15.349	14.853	0.565	0	3.318	24.779	1.000	15.3	+
Inact8	13.099	26.326	15.409	-0.094	0	7.518	-30.988	1.000	14.4	-
Inact9	10.006	20.443	15.141	0	0	6.102	-12.801	1.000	0.4	-
Inact11	10.203	20.728	15.247	0.101	0	5.973	-10.763	1.000	1.1	-
Inact18	10.249	21.555	15.207	0.115	0	5.773	-17.312	1.000	3.0	-
Inact24	9.874	20.648	15.071	0	0	5.527	-13.928	1.000	2.1	-
Inact26	11.681	24.046	15.712	-0.121	12.36	7.308	-19.835	1.000	22.8	-
PGE-5215205	3.637	8.098	11.728	0	0	1.724	-4.952	0.993	24.8	-

Table S4. LDA results and classification of the compounds for DF2.

Compound	$^4\chi_c^v$	n_{class}	^0C	^2C	DF2	Prob.	Mahalanobis	Clas.
Act2	0	13	1.337	1.833	5.859	0.997	0.4	+
Act3	0	14	1.334	1.794	6.334	0.998	0.6	+
Act5	0	14	1.319	1.763	5.500	0.996	0.3	+
Act6	0	16	1.330	1.786	4.250	0.986	1.1	+
Act8	0	14	1.334	1.809	5.619	0.996	0.4	+
Act9	0	16	1.344	1.829	4.421	0.988	1.4	+
Act13	0	13	1.302	1.721	5.509	0.996	0.2	+
Act15	0	16	1.302	1.742	1.852	0.864	1.3	+
Act16	0	14	1.346	1.834	6.311	0.998	0.9	+
Act17	0	13	1.346	1.809	8.305	1.000	1.6	+
Act19	0	16	1.340	1.819	4.258	0.986	1.3	+
Act20	0	13	1.362	1.863	8.481	1.000	2.2	+
Act21	0	14	1.346	1.851	5.532	0.996	0.7	+
Act22	0	16	1.354	1.865	4.387	0.988	1.8	+
Act26	0	21	1.351	1.920	-3.228	0.038	10.9	-
Act32	0.125	14	1.299	1.660	-0.122	0.469	17.5	-
Besifloxacin	0	11	1.244	1.572	5.006	0.993	3.5	+
Clinafloxacin	0	11	1.269	1.629	6.265	0.998	2.0	+
Delafloxacin	0	12	1.402	1.977	10.478	1.000	6.2	+
Enoxacin	0	11	1.307	1.307	1.475	0.814	4.8	+
Fleroxacin	0	12	1.345	1.344	8.171	1.000	1.3	+
Gatifloxacin	0	11	1.262	1.262	3.154	0.959	2.7	+
Gemifloxacin	0	13	1.311	1.310	5.241	0.995	0.0	+
Grepafloxacin	0	11	1.249	1.249	3.599	0.973	3.2	+
Lomefloxacin	0	11	1.309	1.309	5.153	0.994	0.8	+
Norfloxacin	0	11	1.293	1.293	1.781	0.856	3.8	+
Ofloxacin	0	12	1.268	1.268	1.386	0.800	3.2	+
Pradofloxacin	0	12	1.282	1.282	9.296	1.000	4.4	+
Sparfloxacin	0	11	1.301	1.300	9.621	1.000	3.0	+
Ulifloxacin	0	11	1.217	1.217	7.474	0.999	9.0	+
PGE-8367769	0	8	1.334	1.334	4.057	0.983	8.1	+
Inact1	0	19	1.357	2.083	-7.856	1.000	8.7	-
Inact2	0	19	1.352	2.053	-7.238	0.999	7.0	-
Inact3	0	20	1.301	1.835	-6.318	0.998	1.0	-
Inact4	0	21	1.278	1.791	-8.756	1.000	1.8	-
Inact5	0	22	1.290	1.778	-7.164	0.999	1.7	-

Inact6	0	18	1.238	1.613	-4.228	0.986	1.5	-
Inact7	0	22	1.289	1.714	-4.435	0.988	2.8	-
Inact10	0	18	1.293	1.787	-3.447	0.969	0.5	-
Inact12	0	19	1.285	1.759	-4.382	0.988	0.3	-
Inact13	0	19	1.293	1.788	-4.434	0.988	0.4	-
Inact14	0	20	1.281	1.693	-2.934	0.949	2.0	-
Inact15	0	20	1.285	1.758	-5.266	0.995	0.5	-
Inact16	0	20	1.293	1.787	-5.318	0.995	0.6	-
Inact17	0	21	1.289	1.694	-2.597	0.931	3.4	-
Inact19	0	20	1.268	1.657	-3.254	0.963	2.1	-
Inact20	0	20	1.227	1.643	-9.080	1.000	2.7	-
Inact21	0	20	1.208	1.616	-10.864	1.000	5.2	-
Inact22	0	21	1.293	1.755	-4.758	0.991	1.4	-
Inact23	0	19	1.235	1.653	-7.417	0.999	1.5	-
Inact25	0	19	1.214	1.581	-7.435	0.999	2.8	-
Inact27	0	20	1.273	1.675	-3.379	0.967	1.8	-
Inact28	0	19	1.221	1.590	-6.802	0.999	2.3	-
Inact29	0	19	1.254	1.637	-3.776	0.978	1.4	-
Inact30	0.125	15	1.292	1.739	-5.337	0.995	13.8	-
Inact31	0.125	15	1.325	1.758	-1.316	0.789	16.3	-
Inact32	0.125	15	1.255	1.639	-7.002	0.999	14.4	-
Inact33	0	14	1.228	1.592	-1.222	0.772	4.5	-
Inact34	0	19	1.275	1.835	-9.459	1.000	3.3	-
Inact35	0	17	1.219	1.687	-9.587	1.000	5.3	-
Inact36	0	18	1.323	1.862	-2.154	0.896	1.9	-
PGE-6116542	0	8	1.301	1.899	1.853	0.136	14.0	+
PGE-9604297	0	7	1.329	1.949	4.929	0.007	18.6	+
Act1	0	14	1.323	1.807	3.920	0.981	0.3	+
Act4	0	13	1.334	1.771	8.302	1.000	1.5	+
Act7	0	13	1.350	1.820	8.538	1.000	1.9	+
Act14	0	14	1.289	1.715	2.959	0.951	0.6	+
Act18	0	14	1.331	1.799	5.472	0.996	0.3	+
Act27	0	20	1.319	1.795	-1.668	0.159	6.5	-
Ciprofloxacin	0	11	1.287	1.701	5.858	0.997	0.9	+
Finafloxacin	0	12	1.307	1.689	8.595	1.000	1.9	+
Garenoxacin	0	13	1.338	1.825	6.511	0.999	0.5	+
Levofloxacin	0	12	1.268	1.713	1.386	0.800	3.2	+
Moxifloxacin	0	12	1.246	1.579	4.004	0.982	3.1	+

Trovafloxacin	0	13	1.389	1.849	13.288	1.000	10.3	+
Inact8	0	23	1.274	1.695	-6.917	0.999	2.8	-
Inact9	0	18	1.285	1.757	-3.391	0.967	0.4	-
Inact11	0	19	1.281	1.694	-2.048	0.886	2.0	-
Inact18	0	20	1.232	1.603	-6.532	0.999	1.9	-
Inact24	0	19	1.272	1.709	-4.165	0.985	0.5	-
Inact26	0	20	1.197	1.561	-10.064	1.000	5.3	-
PGE-5215205	0	7	1.358	1.995	7.379	0.001	22.6	+

Table S5. Theoretically active compounds selected by the prediction model of antibacterial activity against *E. coli* (DF1= 0-32 and *Nclass* = 11-16).

Compound	Activity	DF1	*Nclass*
Aconine	Alcaloid	29.800868	11
Aconitine	Antipyretic	23.4464385	14
Adlumidine	Plant extract	5.37152537	11
Albofungin	Antibacterial agent	17.1846	14
9-aminocamptothecin	Antitumoral	4.64123362	11
Anabsinthin	Plant extract	3.22992963	11
Asperlicin	Plant extract	4.05486582	14
Asperuloside	Anti-inflammatory	4.6412	12
Baknkosin	Plant extract	1.91637848	11
Balofloxacin	Antibacterial agent	10.6166	12
Baptigenin	Plant extract	5.8222	11
Bicuculline	GABA Antagonist	5.37152537	11
Bis(4-amino-1-anthraquinonyl)amine	Plant extract	0.6841	14
Brequinar	Antitumoral	11.2589198	14
Brucine	Plant extract	22.8943611	11
Camptothecin	10.3Antitumoral	7.46488877	11
Carminic acid	Pigment	13.3912435	13
Cervicarcin	Antitumoral	1.43479591	11
Cevine	Plant extract	8.4642941	12
Chlorophacinone	Pesticide	14.7436	11
Cichorin	Plant extract	24.5077405	11
Cinolazepam	Sedative	10.5092	11
Clocortolone	Corticoid	28.5745441	12
Daidzein	Antioxidant	20.5348	11
Danofloxacin	Antibacterial agent	4.3332	12
Daphinin	Plant extract	2.50387559	11
Delsoline	Plant extract	18.9492644	11
Delcosine	Plant extract	27.2274329	11
Demeclocycline	Antibacterial agent	19.2969	11
Destomycin A	Antibacterial agent	9.82704032	14
Difloxacin	Antibacterial agent	3.7894	13
Diflufenican	Pesticide	17.0194	14

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Difluprednate	Anti-inflammatory	28.6290376	14
Dolasetron	Antiemetic	3.6360	13
Doxacycline	Antibacterial agent	3.90377797	11
Droxicam	Anti-inflammatory	6.0101	11
Elliptone	Antitumoral agent	14.2946905	12
Enrofloxacin	Antibacterial agent	0.3662	13
Florantyrone	Choleretic	6.1612	11
Flumetsulam	Herbicide	7.5798	11
Flumiclorac	Pesticide	6.2391	11
Flumioxazin	Herbicide	16.1175	11
Flunoxaprofen	Anti-inflammatory	27.9084	12
Fluocortolone	Glucocorticoid	1.1966	12
Fluperolone	Glucocorticoid	30.4742166	14
Flurprednisolone	Corticosteroid	23.4515	12
Frangulin A	Laxative	26.6393	13
Genistein	Antitumoral	7.1546	11
Genitopicrin	Plant extract	5.44208396	11
Germine	Plant extract	23.624289	12
Glucofrangulin	Laxantive	2.0069	14
a-Glucogallin	Plant extract	3.2521793	11
b-Glucogallin	Plant extract	3.2521793	11
Halopredone	Anti-inflammatory	25.8426115	14
Halophytine	Plant extract	31.8583805	13
Hygromycin B	Anthelmintic	9.82704032	14
Indaconitine	Plant extract	10.940243	14
Justicidin B	Plant extract	6.40057596	11
Laccaic acid	Pigment	5.20682652	14
Leucodrin	Plant extract	6.94981692	11
Linezolid	Antibacterial agent	31.7005098	14
Loganin	Plant extract	9.65111285	12
Lyxoflavine	Vitamin	23.6352	11
Marbofloxacin	Antibacterial agent	31.7005098	12
Medicagol	Plant extract	24.6561522	11
Melezitose	Carbohydrate	22.8365434	12
Meprednisone	Glucocorticoid	10.5627254	12
Metacycline	Antibacterial agent	30.0751418	11
Minocycline	Antibacterial agent	7.8405858	12
Mometasone	Anti-inflammatory	0.87176752	14
Moxifloxacin	Antibacterial agent	7.8406	12
Nalbuphine	Analgesic	28.3357209	11
Narcotoline	Plant extract	10.1735761	12
Noscapine	Antitussive	15.7870044	12
Ochratoxin A	Mycotoxin	0.5502	14
Paroxetine	Antidepressant	2.00305135	13
Pefloxacin	Antibacterial agent	9.81034608	12
Pipebuzone	Anti-inflammatory	5.8395182	12
Pirazolac	Anti-inflammatory	4.67725356	12

Pirenoxine	Cataract treatment	6.7677	11
Pirenzepine	Anti-ulcer	1.10982539	11
Plumieride	Plant extract	9.5018	12
Prednyldiene	Glucocorticoid	2.8233	12
Pseudobaptigenin	Plant extract	2.94054093	11
Quatrimycin	Antibacterial agent	15.2208	11
Quininone	Anti-malaria	1.7458218	12
Quinoxyfen	Fungicide	13.5283125	11
Rhamnetin	Plant extract	5.1892	11
Rhodomycin B	Vitamin	4.8605	14
Riboflavin	Vitamin	4.1640	11
Ribostamycin	Antibacterial agent	2.43943805	13
Rotenone	Antiparasitic	17.0583372	14
Rubitecan	Topoisomerase inhibitor	3.1031	12
Rufloxacin	Antibacterial agent	30.4049	12
Sancycline	Antibacterial agent	2.21199125	11
Scoparin	Reagent	18.8206	13
Scutellarein	Plant extract	2.5795	11
Sitafloxacin	Antibacterial agent	25.0367	11
Skimmin	Plant extract	5.9765	11
Sporidesmin A	Mycotoxin	18.7458006	11
Swertiamarin	Plant extract	8.0637	12
Tectorigenin	Plant extract	0.7760	11
Temafloxacin	Antibacterial agent	23.3822	12
Tephrosin	Plant extract	24.7192314	14
Tetracycline	Antibacterial agent	13.2993	11
Tetrahydrocortisone	Steroid	10.1895718	12
Topotecan	Antitumoral	5.55463332	13
Tosufloxacin	Antibacterial agent	27.1346	12
Tritoqualine	Antihistaminic	2.46150506	13
Tropisetron	Antiemetic	0.07165887	11
Trovafloxacin	Antibacterial agent	26.8002	13
Verbenalin	Plant extract	14.237474	12
Vindoline	Plant extract	3.73294636	11

Table S6. Theoretically active compounds selected by DF1=0-32 and DF2 = 0-12.

Compound	Activity	DF1	DF2
Aflatoxin B1	Mycotoxin	9.618	1.958
Aflatoxin G1	Mycotoxin	11.559	0.934
Aflatoxin M1	Mycotoxin	12.535	2.979
Afloqualone	Sedative	9.819	2.292

Albofungin	Antibiotic	17.185	1.938
Alizarine Blue	Pigment	22.699	10.918
Amarogentin	Plant extract	2.291	7.186
Amarolide	Plant extract	1.043	4.068
1-Aminoanthraquinone	Plant extract	10.378	9.906
1-Aminoanthraquinone-2-carboxylic Acid	Plant extract	4.241	13.995
9-Aminocamptothecin	Antitumoral	4.641	0.705
Anagyrine	Antitumoral	0.654	0.925
Anilinephthalein	Laxative	8.941	0.814
Anisindione	Anticoagulant	0.406	1.861
Anthralin	Epithelium recovery	4.225	11.037
Anthraquinone	Plant extract	11.361	7.597
Anthrone	Pigment	8.565	2.751
Apigetrin	Plant extract	4.021	8.722
Ascorbigen	Analgesic	12.955	8.936
Asperuloside	Anti-inflammatory	10.617	12.004
Balofloxacin	Antibiotic	5.822	2.159
Baptigenin	Plant extract	0.684	10.734
Benzanthrone	Pigment	24.204	1.888
Benzotrifluoride	Reagent	2.722	9.268
Bis(4-amino-1-anthraquinonyl)amine	Plant extract	14.744	3.637
Bostycoidin	Antibiotic	2.152	5.667
Cacotheline	PH indicator de pH	8.485	11.067
Capecitabine	Antitumoral	3.260	2.162
Carbamazepine	Anticonvulsivo	2.293	1.411
Catalposide	Plant extract	16.829	9.558
Chartreusin	Antibiotic	18.747	0.597
p-Chlorobenzotrifluoride	Disolvente	0.036	4.983
Chlorophacinone	Pesticida	10.509	2.361
Chrysophanic Acid	Antitumoral	3.613	11.098
Cinolazepam	Sedative	20.535	2.909
Clorindione	Anticoagulant	7.082	2.688
Coriamyrtin	Plant extract	10.060	2.745
Coumestrol	Estrógeno	18.284	4.224
Cyclic AMP	Bioquímica	0.566	8.623
Cyclic GMP	Bioquímica	5.844	11.099
Cytisine	Deshabituación tabáquica	2.143	5.982
Daidzein	Antioxidante	4.333	3.781
Daidzin	Plant extract	10.111	7.826
Danofloxacin	Antibiotic	19.297	5.084
Demeclocycline	Antibiotic	3.789	13.391
DFDD	Reagent	9.992	2.475
Difloxacin	Antibiotic	17.019	2.198
Diflufenican	Pesticida	3.636	1.121
p-Difluorobenzene	Reagent	13.717	11.182
4,4'-Difluorodiphenyl	Reagent	13.834	4.032
Diphenadione	Pesticida	11.710	5.941
Dolasetron	Antiemético	6.010	1.029
Doxefazepam	Sedative	23.886	3.308
Doxenitoin	Anticonvulsivo	1.347	0.065
Droxicam	Anti-inflammatory	0.366	10.286
Efavirenz	Antirretroviral	15.277	6.834

Emodin	Plant extract	3.495	13.836
Enrofloxacin	Antibiotic	6.161	0.562
Fialuridine	Antiviral	21.908	2.047
Florantyrone	Colerético	7.579	2.298
Fluconazole	Antifúngico	0.171	2.875
Flucytosine	Antifúngico	13.759	9.461
Fludioxonil	Antifúngico	23.124	5.194
Fluindione	Anticoagulant	18.360	10.631
Flumequine	Antibiotic	21.524	12.749
Flumetsulam	Herbicida	6.239	8.265
Flumiclorac	Pesticida	16.117	5.789
Flumioxazin	Herbicida	27.908	7.576
Flunitrazepam	Sedative	13.288	4.558
Flunoxaprofen	Anti-inflammatory	1.197	0.873
Fluocortolone	Glucocorticoide	23.452	0.267
Fluorescamine	Reagent	18.442	1.999
Fluorescein	Pigment	25.072	3.622
p-Fluoroaniline	Reagent	13.212	8.286
p-Fluorophenylacetic Acid	Reagent	6.264	12.133
o-Fluorotoluene	Reagent	9.259	1.824
m-Fluorotoluene	Reagent	5.390	2.597
p-Fluorotoluene	Reagent	9.311	3.750
Fluprednisolone	Corticosteroide	26.639	2.575
Flurbiprofen	Anti-inflammatory	14.648	5.300
Fluroxypyr	Herbicida	2.846	1.372
Flutriafol	Antifúngico	13.144	3.853
Frangulin A	Laxative	7.155	9.696
Frenolicin	Antiparasitario	4.828	8.867
Fustin	Neuroprotector	7.058	13.472
Gallein	Pigment	24.412	10.141
Genistein	Antitumoral	2.007	6.992
Gentisin	Antiviral	5.527	1.451
Gibberellic Acid	Fertilizante	30.002	5.712
Glitoxin	Inmunosupresor	9.067	3.585
Glucofrangulin A	Laxative	23.635	11.657
Hematein	Pigment	3.157	11.289
Hydromorphone	Opioide	20.049	2.054
Ibafloxacin	Antibiotic	18.183	9.465
Indanthrene®	Pigment	31.605	0.605
Indigo	Pigment	13.425	3.415
Isatide	Plant extract	24.274	10.064
Isoapo-b-erythroidine	Plant extract	6.432	0.785
Isolysergic Acid	Mycotoxin	4.916	3.877
Kaempferitrin	Plant extract	14.571	7.671
Kaempferol	Plant extract	0.769	10.628
Lufenuron	Pesticida	1.580	3.299
Luteolin	Plant extract	5.221	10.116
Lyxoflavine	Vitamina	4.753	8.181
Mefloquine (Hydrochloride)	Antimalárico	8.442	11.944
Minocycline	Antibiotic	7.841	8.446
Mitomycin C	Antitumoral	18.701	8.687
Morphine	Opioide	17.945	2.699
Moxifloxacin	Antibiotic	24.496	4.004
Naloxone	Antagonista opioide	23.532	3.191

Naltrexone	Antagonista opioide	21.426	0.985
1,4-Naphthoquinone	Plant extract	1.274	10.704
Naringin	Edulcorante	10.094	6.304
Nevirapine	Antirretroviral	6.738	0.305
Niflumic Acid	Anti-inflammatory	1.552	6.326
Nivalenol	Mycotoxin	23.403	12.953
Normorphine	Opioide	16.243	6.101
Nybomycin	Antiviral	11.526	1.667
Ochratoxin A	Mycotoxin	0.550	1.469
Parvaquone	Antimalárico	3.785	9.887
Phanquinone	Antibiotic	3.144	7.081
Phenanthrenequinone	Pigment	11.628	7.597
Phenindione	Anticoagulant	8.812	7.509
Phenolphthalein	pH indicator	13.187	2.809
Phenytoin	Anticonvulsant	6.540	3.795
Phloridzin	Plant extract	8.333	10.775
Phorbol	Reagent	8.466	2.659
Picrotin	Antidote	27.510	1.635
Pirenoxine	Cataract treatment	6.768	4.632
Pleurotin(e)	Antibiotic	23.089	6.937
Plumieride	Plant extract	9.502	9.842
Polyoxin A	Antibiotic	9.308	13.504
Porfiromycin	Antitumoral	10.050	6.506
Prenylidene	Glucocorticoid	2.823	0.664
Praquiloside	Phytotoxin	15.896	4.538
Quatrimycin	Antibiotic	15.221	11.019
Quercetin	Nutritional supplement	10.659	13.791
Quinoline Yellow Spirit Soluble	Pigment	19.567	3.226
Rhamnetin	Plant extract	5.189	5.750
Rheochrysdin	Plant extract	12.872	10.868
Rhodomycin B	Plant extract	4.860	2.477
Riboflavin	Vitamin	4.164	8.181
Rolitetracycline	Antibiotic	11.944	1.408
Ruberythric Acid	Pigment	31.628	9.565
Rubitecan	Topoisomerase inhibitor	3.103	2.746
Rufloxacin	Antibiotic	30.405	1.920
Samaderin A	Plant extract	27.932	3.512
Santonic Acid	Reagent	9.248	7.186
Scoparin	Reagent	18.821	11.310
Scutellarein	Plant extract	2.579	9.906
Silymarin (Silybin)	Hepatoprotector	9.201	2.780
Sitafloxacin	Antibiotic	25.037	5.695
Skimmin	Plant extract	5.976	12.474
Sophorabioside	Plant extract	20.341	3.322
Sorbinil	Aldose reductase inhibitor	30.107	10.312
Spectinomycin	Antibiotic	9.085	8.145
Swetiamarin	Plant extract	8.064	13.759
Tazobactam	Antibiotic	7.542	13.804
Tectorigenin	Plant extract	0.776	3.647
Tegafur	Antitumoral	6.778	12.566
Temafloxacin	Antibiotic	23.382	6.824
Tetracycline	Antibiotic	13.299	11.019
Tetrantoin	Anticonvulsant	9.523	5.549
Theaflavine	Antioxidant	14.521	10.273

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Thiazopyr	Herbicide	3.995	10.359
Thioxanthone	Printing product	10.137	3.000
Tosufloxacin	Antibiotic	27.135	10.909
Trovafloxacin	Antibiotic	26.800	13.288
Truxillic acid	Reagent	8.467	13.039
Vellosimine	Plant extract	9.002	0.168
Viridin	Antifungal	21.757	4.967
Vomitoxin	Mycotoxin	4.228	7.937
Voriconazole	Antifungal	7.369	5.230

Group	Active	Inactive	Accuracy (%)
Training active	29	2	93.5
Training inactive	0	32	100
Test active	11	1	91.7
Test inactive	0	7	100
TOTAL	**40**	**20**	**96.3**

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Group	Active	Inactive	Accuracy (%)
Training active	20	11	64.5
Training inactive	0	32	100
Test active	11	1	91.7
Test inactive	0	7	100
TOTAL	**31**	**51**	**89.1**