Synthesis and in vitro cytotoxic effect of 6-amino-substituted 11*H*- and 11Me-indolo[3,2-*c*]quinolines

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ABSTRACT

A series of 6-amino-11*H*- indolo[3,2-*c*]quinoline derivatives with various substituents on the quinoline ring were synthesized. A methyl group introduced to N-11 of the intermediate **4** to elaborate novel analogue **7**. The cytotoxic effect of these 6-amino-substituted 11*H*- and 11-methyl-indolo[3,2-*c*]quinoline derivatives *in vitro* were tested against MV4-11 (human leukemia), A549 (non-small cell lung cancer) and HCT116 (colon cancer) and BALB/3T3 (normal murine fibroblasts). All the *N*-11 methylated compounds significantly increased the cytotoxicity. Compound **7p** was most active with the IC₅₀ value of 0.052 μM against the MV4-11 cell line, and also exhibited a selective activity against A549, HCT116 and BALB/3T3 cell line, with the respective IC₅₀ values of 0.112, 0.007 and 0.083 μM, which were higher or comparable to those of the anticancer drug doxorubicin HCl. The binding constants of **5g** and **7h** to salmon fish sperm DNA were also evaluated using UV-vis absorption spectroscopy, indicating intercalation binding with constants of 1.05 × 10⁶ L/mol and

4.84×10^6 L/mol.

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1. Introduction

DNA has been a major target for anticancer drug interactions because of the ability to interfere with transcription and DNA replication [1]. Successful examples are doxorubicin [2] and other polycyclic aromatics [3,4]. A large variety of anticanceragents are associated with severe side effects and reduced clinical efficacy, and hence development of alternative potential anticancer drugs is always in demand.

Alkaloids from natural sources have been used as the drug or the lead for the development of more potent anticancer agents [5–7]. The biological activities of indoloquinolines isolated from the root of *Cryptolepis sanguinolenta*, the climbing shrub growing in some African countries, have recently been intensely studied [8–10], because the aqueous macerate or decoction of this root is used in traditional medicine for the treatment of malaria and various disorders of the body [11,12]. For example, the representative constituent of cryptolepine **i** (5-methylindolo[3,2-*b*]quinoline), and neocryptolepine **ii** (5-methylindolo[2,3-*b*]quinoline) (Figure 1) have been shown to possess a broad spectrum of biological activities including antibacterial [13,14], antifungal [13,14], and antimalarial [15–18]. These significant biological properties can be ascribed to their linearly arranged tetracyclic planar structures, which can intercalate DNA and inhibit topoisomerase II, revealing a high level of cytotoxicity [19–21].

In contrast, another minor constituent, isocryptolepine **iii** (5-methylindolo[2,3-*c*]quinoline) [16,22], and its C2, C3, and C8 substituted derivatives [23], featured by a slightly angled shape compared with the former two

compounds, were tested against CQS (3D7) and CQR (W2mef) *P. falciparum*, showing $IC_{50} = 57$ and 85 nM, respectively, with the 8-bromo-2-chloro derivative. However the other biological properties of **iii** were not well evaluated in comparison to **i** and **ii**. On the other hand, the SAR studies have been achieved on the related structure of the indolo[3,2-*c*]quinolines **iv** to develop for more active drug candidates.

< Fig. 1.>

Planar 3-chloroindolo[3,2-*c*]quinoline derivatives with substituents at C8 and C9 were synthesized by Ibrahim *et al.* to examine the intercalation with DNA, and some showed a significant inhibition of the RNA synthesis[24,25].

6-(*N,N*-dialkylamino)alkyleneaminoindolo[3,2-*c*]quinoline derivatives with a substituent at C8 were claimed in a patent by Brass *et al.*, showing the ID_{50} (50 % inhibition concns.), tested on the culture of mouse leukemia L 1210 tumor cells, that ranged from 0.04 - 2.6 $\mu\text{mol/L}$ [26]. Chen reported that the 6-anilino-11*H*-indolo[3,2-*c*]quinoline derivatives for the *in vitro* antiproliferative evaluation against a 3-cell line panel consisting of MCF7 (breast), NCI-H460 (lung), and SF-268 (CNS), showed the mean GI_{50} value of 1.7 – 1.35 μM with the most active ones [27]. Tzeng reported the synthesis of 6-alkylamino-11*H*-indolo[3,2-*c*]quinolines and their twin derivatives for their antiproliferative activity against several cancer cells[28].

In contrast to these remarkable advancements in the basic SAR search with the 11*H*-indolo[3,2-*c*]quinoline derivatives **iv**, the testing with the 11Me-indolo[3,2-*c*]quinoline derivatives **v**, the congener and non-natural type isocryptolepines, have not been undertaken at all. In our previous paper, we demonstrated that presence and position of the *N*-Me group in the indolo[2,3-*b*]quinoline (neocryptolepine) core is highly efficacious for the antiparasmodial and antiproliferative activities [29–33]. For example, the antiparasmodial activity of the indolo[2,3-*b*]quinoline derivatives with or without the

N-methyl group was assigned in the order of 5-methylated > no methylated > 6-methylated [29]. A similar trend of activity was found in the cytotoxic properties of the indolo[2,3-*b*]quinoline derivatives [32].

In this paper, we describe the cytotoxic effect of a series of 11*H*-indolo[3,2-*c*]quinoline derivatives **iv** with various alkylamino groups at C6 along with various substituents at C2. Furthermore, we examined the cytotoxicity of a series of 11Me-indolo[3,2-*c*]quinoline derivatives **v** and surveyed the effect of the *N*-Me group on this activity [34].

2. Results and discussion

2.1. Chemistry

As shown in Scheme 1, the 11*H*- and 11Me-indolo[3,2-*c*]quinoline cores **4** and **7** were prepared by the method described by Bergman [35], and Tzeng [28], and us with modification [34]. Thus, the isatins **1** were combined with 2-aminobenzylamine (**2**) by heating in acetic acid, producing the 6-dihydro-11*H*-indolo[3,2-*c*]quinoline-6(5*H*)-ones **3**. Compound **3** was then obtained and converted to 6-chloro-11*H*-indolo[3,2-*c*]quinoline **4** by dehydrative chlorination with POCl₃. Furthermore, the treatment of **4** with sodium hydride followed with iodomethane in the DMF afforded 6-chloro-11-methyl-indolo[3,2-*c*]quinoline **6** as a result of the selective methylation at the nitrogen of the indole ring. Subsequently, the aminations of **4** and **6** with the appropriate amines were attempted with heating. Thus, the 6-chloro-11*H*-indolo[3,2-*c*]quinoline **4** underwent the addition-elimination reaction of the alkyl amines and anilines by conventional heating within 20 min to 4 h in fairly good yields. On the other hand, the amination of the 6-chloro-11-methyl-indolo[3,2-*c*]quinoline congeners **6** were successful at the elevated temperature of 140 °C for a longer reaction time (24 h), giving the

corresponding amine adducts **7** in slightly lower yields. However, the application of MW irradiation improved the reaction time to 10 h. Further modification of the 6-aminoalkylamino derivative **7a** was easily achieved by mixing with phenylisocyanate in THF at room temperature, producing the urea derivative **8**.

< **Scheme 1.** >

3. Biological tests

3.1. Cytotoxic activity in vitro against MV4-11 A549, HCT116 and BALB/3T3 cell lines.

Table 1 shows the cytotoxic effect of the synthesized compound **5** against the human leukemia MV4-11 cell line, with varying the substituents at C2. All the assayed compounds, except for the **5l**, **5n** and **5o**, were cytotoxic against the MV4-11 leukemia cells (IC_{50} below 0.9 μ M), and exhibited higher cytotoxicity than the reference anticancer drug, cisplatin (IC_{50} 2.363 μ M). Among compounds, **5t** which showed the highest cytotoxic effect (IC_{50} 0.115 μ M), that was modified with the 3-aminopropylamino group at the C6 and a methoxy at C2. The more potent compounds were **5a**, **5s** and **5u** with IC_{50} values below 0.2 μ M. This result demonstrated that the 3-aminopropylamino groups at C6 was an essential and effective substituent that led to relatively higher activities than the other substituent group (**5b–5o**). The compounds bearing phenylamino groups (**5n**, **5o**) showed the lowest activities. The halogen substituent at C2 significantly reduced the cytotoxicity. In addition, it turned out that linear amino derivatives were more active than the cyclic amino derivatives (**5f**, **5h**, **5k**, **5l**).

Consequently, compounds **5a–5k**, **5m** and **5s–5u** were examined for their cytotoxicity against the non-small cell lung cancer (A549) and colon cancer (HCT116) cell lines, along with normal murine fibroblasts (BALB/3T3). As listed in Table 2, all the tested compounds were cytotoxic against the A549 and HCT16 cancer cells, and their activities against the cancer cell were much higher than the activity of cisplatin used as the control agent. Although the compounds **5a**, **5s**, **5t** and **5u** appeared high

active against A549 and also HCT116 cancer cell lines, they possessed a lower cytotoxicity against the normal murine fibroblasts cell BALB/3T3. Compounds **5s** and **5t** substituted by methyl and methoxy in the quinoline ring with the IC₅₀ values of 0.076-0.072 μ M against the HCT116 cancer cells, expressed about 8-9 times higher activity compared to MV4-11 cells. Compounds **5i** and **5j** bearing the 6-aminoalkylhydroxyl group showed a selective cytotoxic effect mostly against the HCT116 cell line, while their activities were about 7-9 times higher than against the A549 cancer cell line. For the cyclic amino substituted agents **5f**, **5h** and **5m**, they exhibited higher cytotoxicity against the normal murine fibroblasts cell BALB/3T3, and showed a selective cytotoxic effect against the MV4-11 cell line.

Similarly, the 11-methyl-indolo[3,2-*c*]quinoline derivatives were examined for the cytotoxicity against the human leukemia MV4-11 cell line, the results of which display in Table 3. Among the no substituted compounds at C2 position, the 6-aminoheptylaminodiethyl derivative **7d** exhibited the most activity with an IC₅₀ of 0.072 μ M. Noteworthy is the remarkably increased activity of **7p** (IC₅₀ 0.052 μ M) substituted with the electron-withdrawing NO₂ at the C2 position compared to the no substituted **7a**. Besides, introduction of the electron-donating groups Me and MeO, was more favorable (**7n**, **7o**). On the contrary, for the 3-aminoalkylamino substituent **7a**, **7f**, **7j** and **7m**, the cytotoxicity decreased when the H at C2 was changed by a halogen. The same trend was observed in compounds **7b**, **7g** and **7k** as well. The 2-chloro-6-aminopropylaminodimethyl derivative **7h** was significantly more active than the C2-H analogue **7c**. Unfortunately the compound bearing urea **8** was less active than **7a**.

We clearly determined that the cytotoxicity of all the 11-methyl-indolo[3,2-*c*]quinoline derivatives **7** were higher than the *N*-11 demethylated **5**, with the IC₅₀ less than 0.75 μ M against the A549 cancer cell and IC₅₀ less than 0.2 μ M against the HCT116 cancer cell (Table 4). Moreover, all the test compounds significantly increased the selective cytotoxic effect against the HCT116 coloncancer cells. Compounds **7o** and **7p** exhibited excellent activities against the HCT116 cell line with the respective IC₅₀ values of 0.008 and 0.007 μ M.

<Table 1.>

< Table 2.>

< Table 3.>

< Table 4.>

3.2. Spectroscopic characterizations of **5g** and **7h** interacting with DNA

UV–visible spectroscopy is the most common and convenient way to study interaction between small molecule and nucleic acid. Generally, red shift (or blue shift) and hypochromic (or hyperchromic) effect are observed in the absorption spectra if molecules interact with DNA.[32]

The DNA binding study of **5g** and **7h** was performed using UV-vis absorption spectroscopy with salmon fish sperm DNA in phosphate buffer (pH 7.0) at 20 °C. The blue and hyperchromic effect was observed in the absorption spectra, while the DNA solution was gradually added to the compound solution. The results in Fig. 2 (a) and (c) showed that the absorption band at 257 nm for **5g** and **7h** increased while increasing the DNA concentration. The maximum absorption shifts from 257 nm to a longer wavelength at 270 nm (the maximum absorption wavelength of DNA is 260 nm). It is illustrated that there is a strong interaction between **5g** and **7h** and DNA. The binding constant of **5g**-DNA was calculated as 1.05×10^6 L/mol and **7h**-DNA was then calculated as 4.84×10^6 L/mol according to double-reciprocal equation. The result that all the 11-methyl-indolo[3,2-*c*]quinolines showed higher cytotoxicity against the cancer lines than the 11*H*-indolo[3,2-*c*]quinolines, is explained by that compound **7h** showed slightly stronger activity of interacting with DNA than the compound **5g**.

< Fig. 2.>

4. Conclusion

We prepared a series of 6-amino-substituted 11*H*- indolo[3,2-*c*]quinolines **5**, and *in vitro* evaluated their cytotoxic effect. The 3-aminopropylamino group can favor the activity of the indolo[3,2-*c*]quinoline at C6. We then have designed and synthesized a novel series of 6-aminoalkylamino-substituted 11-methyl- indolo[3,2-*c*]quinolineS **7**. As a result of a SAR study of the all compounds, we confirmed that the introduced methyl group to *N*-11 was significantly efficacious regarding the cytotoxicity. Some compounds showed a very high cytotoxic effect, especially compound **7p**, which exhibited an excellent activity against the human leukemia MV4-11 cell line (IC₅₀ 0.052 μ M) and HCT116 cancer cell line (IC₅₀ 0.007 μ M). In the DNA interaction experiment, 11-methyl compound slightly heighten the DNA intercalating constant compared to 11*H*-derivative.

5. EXPERIMENTAL

5.1. General and methods

The commercially obtained reagents were directly used without further purification. The ¹H NMR and ¹³C NMR spectra were measured by a Varian INOVA-600 spectrometer with DMSO-*d*₆ as the solvent unless otherwise indicated. Melting points were determined using a J-Science RFS-10 hot stage microscope. Elemental analyses were measured by a Perkin-Elmer 2400 II elemental analyzer. High resolution mass spectra were obtained on a Bruker micrOTOF II-SKA spectrometer.

5.2. Chemistry

5.2.1. General procedure for the synthesis of

*N*¹-(11*H*-indolo[3,2-*c*]quinolin-6-yl)propane-1,3-diamine (**5a**)

6-Chloroindolo[3,2-*c*]quinoline (**4a**, 0.4 mmol) and an excess of the appropriate amine (2.0 mmol) were heated together at 90–100 °C for 20 min. The progress was monitored by TLC to ensure completion of the reaction. The reaction mixture was then added to water, and the formed solids were collected by filtration. The crude product was purified by flash chromatography using AcOEt-2N ammonia in MeOH (10:1 V/V) as the eluent to yield the pure **5a**[34]. Yield: 93%, Mp: >230 °C decompose; ¹H NMR δ 8.42 (d, *J*= 7.9 Hz, 1H), 8.25 (d, *J*= 7.9 Hz, 1H), 7.65 (d, *J*= 8.1 Hz, 2H), 7.48 (dd, *J*= 8.2, 7.0 Hz, 1H), 7.40 (t, *J*= 7.6 Hz, 1H), 7.27 (dt, *J*= 14.6, 7.4 Hz, 2H), 7.07 (s, 1H), 3.80 (t, *J*= 5.9 Hz, 2H), 2.75 (t, *J*= 5.7 Hz, 2H), 1.83 (m, 2H); ¹³C NMR δ 153.4, 146.6, 141.1, 138.5, 128.4, 126.6, 124.3, 122.0, 121.9, 121.0 (2C), 120.5, 114.5, 111.8, 103.1, 40.5 39.6, 32.0. ESI-HRMS: *m/z* calcd. for C₁₈H₁₈N₄[M-H]⁺ 289.1453. Found 289.1456.

5.2.2. *N*¹-(11*H*-Indolo[3,2-*c*]quinolin-6-yl)butane-1,4-diamine (**5b**)

Yield: 78%, Mp: 166–168 °C; ¹H NMR δ 8.40 (d, *J*= 7.6 Hz, 1H), 8.25 (d, *J*= 7.6 Hz, 1H), 7.66 (d, *J*= 6.9 Hz, 2H), 7.48 (t, *J*= 7.3 Hz, 1H), 7.41 (t, *J*= 7.3 Hz, 1H), 7.27 (dt, *J*= 17.1, 7.2 Hz, 2H), 6.62 (s, 1H), 3.72 (s, 2H), 2.64 (t, *J*= 6.6 Hz, 2H), 1.78 (m, 2H), 1.52 (dd, *J*= 13.5, 6.7 Hz, 2H); ¹³C NMR δ 153.4, 146.6, 141.2, 138.5, 128.4, 126.7, 124.3, 122.0, 121.9, 121.2, 121.1, 120.5, 114.5, 111.8, 103.2, 42.0, 40.8, 31.4, 27.3. ESI-HRMS: *m/z* calcd. for C₁₉H₂₀N₄[M-H]⁺ 303.1610. Found 303.1614.

5.2.3. *N*¹-(11*H*-Indolo[3,2-*c*]quinolin-6-yl)pentane-1,5-diamine (**5c**)

Yield: 80%, Mp: 168–169 °C; ¹H NMR δ 8.41 (d, *J*= 7.6 Hz, 1H), 8.26 (m, 1H), 7.66 (d, *J*= 7.2 Hz, 2H), 7.49 (t, *J*= 7.1 Hz, 1H), 7.41 (t, *J*= 7.4 Hz, 1H), 7.28 (dt, *J*= 14.9, 7.2 Hz, 2H), 6.56 (s, 1H), 3.72 (s, 2H), 2.56 (s, 2H), 1.77 (d, *J*= 5.4 Hz, 2H),

1.43 (s, 4H); ^{13}C NMR δ 153.4, 146.6, 141.2, 138.5, 128.4, 126.7, 124.3, 122.0, 121.9, 121.2, 121.1, 120.5, 114.5, 111.8, 103.2, 42.2, 41.0, 33.8, 29.8, 24.6.ESI-HRMS: m/z calcd. for $\text{C}_{20}\text{H}_{22}\text{N}_4[\text{M-H}]^+$ 317.1766. Found 317.1761.

5.2.4. *N*¹-(11*H*-Indolo[3,2-*c*]quinolin-6-yl)hexane-1,6-diamine(**5d**)

Yield: 78%; ^1H NMR δ 8.38 (d, J = 7.9 Hz, 1H), 8.23 (d, J = 7.7 Hz, 1H), 7.64 (d, J = 8.1 Hz, 2H), 7.47 (dd, J = 11.2, 4.0 Hz, 1H), 7.40 (t, J = 7.5 Hz, 1H), 7.27 (dt, J = 18.5, 7.4 Hz, 2H), 6.54 (d, J = 5.5 Hz, 1H), 3.69 (dd, J = 13.1, 6.6 Hz, 2H), 2.51 (d, J = 5.9 Hz, 2H), 1.75 (t, J = 6.9 Hz, 2H), 1.40 (m, 6H); ^{13}C NMR δ 153.4, 146.6, 141.2, 138.5, 128.4, 126.7, 124.3, 121.9, 121.8, 121.2, 121.1, 120.5, 114.5, 111.8, 103.2, 42.1, 40.9, 33.8, 29.9, 27.1, 26.8.ESI-HRMS: m/z calcd. for $\text{C}_{21}\text{H}_{24}\text{N}_4[\text{M-H}]^+$ 331.1923. Found 331.1916.

5.2.5.

N-(3-(4-(3-Aminopropyl)piperazin-1-yl)propyl)-11*H*-indolo[3,2-*c*]quinolin-6-amine (**5e**)

Yield:47%; ^1H NMR δ 12.47 (s, 1H), 8.36 (d, J = 8.0 Hz, 1H), 8.23 (dd, J = 7.9, 1.1 Hz, 1H), 7.63 (dd, J = 10.8, 8.2 Hz, 2H), 7.48 (d, J = 1.4 Hz, 1H), 7.41 (s, 1H), 7.33–7.22 (m, 2H), 6.64 (s, 1H), 3.72 (d, J = 6.1 Hz, 2H), 2.53 (t, J = 6.7 Hz, 4H), 2.44 (t, J = 6.7 Hz, 6H), 2.34–2.23 (m, 4H), 1.95–1.85 (m, 2H), 1.54–1.42 (m, 2H); ^{13}C NMR δ 153.4, 146.5, 141.1, 138.5, 128.4, 126.6, 124.3, 121.93, 121.8, 121.2 (2C), 120.9, 114.5, 111.8, 103.2, 57.1 (2C), 56.3, 53.6 (2C), 53.2 (2C), 30.7, 26.5 (2C).ESI-HRMS: m/z calcd. for $\text{C}_{25}\text{H}_{32}\text{N}_6[\text{M-H}]^+$ 415.2610. Found 415.2609.

5.2.6. 6-(1,4-Diazepan-1-yl)-11*H*-indolo[3,2-*c*]quinoline (**5f**)

Yield: 83%, Mp: 216–218 °C; ^1H NMR δ 12.61 (s, 1H), 8.35 (d, J = 8.0 Hz, 1H), 8.02 (d, J = 7.9 Hz, 1H), 7.77 (d, J = 8.3 Hz, 1H), 7.68 (d, J = 8.0 Hz, 1H), 7.56 (dd, J = 8.1, 7.1 Hz, 1H), 7.42 (m, 2H), 7.31 (t, J = 7.5 Hz, 1H), 3.86 (s, 2H), 3.80 (d, J = 2.3 Hz, 2H), 2.98 (d, J = 2.3 Hz, 2H), 2.88 (t, J = 5.6 Hz, 2H), 1.88 (s, 2H); ^{13}C NMR δ 157.6, 145.1, 142.7, 138.9, 128.6, 127.7, 124.6, 123.0, 122.5, 122.1, 122.0, 120.7,

115.5, 112.0, 106.0, 55.4, 50.7, 49.1, 48.6, 31.1. ESI-HRMS: m/z calcd. for $C_{20}H_{20}N_4[M-H]^+$ 315.1610. Found 315.1608.

5.2.7. *N¹-(11H-Indolo[3,2-c]quinolin-6-yl)-N³,N³-dimethylpropane-1,3-diamine (5g)*

Yield: 90%; 1H NMR δ 12.45 (s, 1H), 8.25 (t, J = 8.1 Hz, 2H), 7.66 (d, J = 8.0 Hz, 2H), 7.48 (t, J = 7.6 Hz, 1H), 7.40 (t, J = 7.6 Hz, 1H), 7.31 (t, J = 7.5 Hz, 1H), 7.26 (t, J = 7.4 Hz, 1H), 7.14 (s, 1H), 3.75 (dd, J = 11.4, 5.9 Hz, 2H), 2.46 (t, J = 6.2 Hz, 2H), 2.24 (s, 6H), 1.89 (dd, J = 12.7, 6.3 Hz, 2H); ^{13}C NMR δ 153.4, 146.7, 141.2, 138.6, 128.5, 126.7, 124.3, 122.0, 122.0, 121.2, 120.6, 120.5, 114.6, 112.0, 103.2, 58.9, 45.8 (2C), 41.0, 26.7. ESI-HRMS: m/z calcd. for $C_{20}H_{22}N_4[M-H]^+$ 317.1766. Found 317.1759.

5.2.8. *6-(4-Methyl-1,4-diazepan-1-yl)-11H-indolo[3,2-c]quinoline (5h)*

Yield: 52%, Mp: 77–79°C; 1H NMR δ 12.59 (s, 1H), 8.34 (d, J = 8.0 Hz, 1H), 8.00 (d, J = 8.0 Hz, 1H), 7.77 (d, J = 8.3 Hz, 1H), 7.67 (d, J = 8.1 Hz, 1H), 7.56 (dd, J = 8.3, 7.0 Hz, 1H), 7.41 (ddd, J = 11.2, 10.6, 7.5 Hz, 2H), 7.31 (t, J = 7.5 Hz, 1H), 3.96–3.88 (m, 2H), 3.88–3.81 (m, 2H), 2.72–2.67 (m, 2H), 2.67–2.60 (m, 2H), 2.29 (s, 3H), 1.97 (dd, J = 8.4, 3.0 Hz, 2H); ^{13}C NMR δ 157.4, 145.3, 142.9, 139.0, 128.8, 127.8, 124.8, 123.1, 122.6, 122.2, 122.2, 120.9, 115.6, 112.1, 106.1, 58.8, 57.1, 52.0, 51.0, 47.1, 27.7.

5.2.9. *2-(11H-Indolo[3,2-c]quinolin-6-ylamino)ethanol (5i)*

Yield: 35%; 1H NMR δ 12.50 (s, 1H), 8.35 (d, J = 7.9 Hz, 1H), 8.26 (d, J = 7.8 Hz, 1H), 7.66 (t, J = 8.8 Hz, 2H), 7.51 (t, J = 7.6 Hz, 1H), 7.42 (t, J = 7.6 Hz, 1H), 7.30 (dd, J = 17.0, 7.8 Hz, 2H), 6.64 (d, J = 5.1 Hz, 1H), 5.41 (s, 1H), 3.80 (m, 2H), 3.75 (t, J = 5.2 Hz, 2H); ^{13}C NMR δ 153.7, 146.2, 141.3, 138.6, 128.7, 126.4, 124.5, 122.1, 121.9, 121.5, 121.1, 120.7, 114.6, 112.0, 103.2, 61.5, 44.2. ESI-HRMS: m/z calcd. for $C_{17}H_{15}N_3O[M-H]^+$ 276.1137. Found 276.1141.

5.2.10. 3-(11H-Indolo[3,2-c]quinolin-6-ylamino)propan-1-ol (**5j**)

Yield: 96%, Mp: 199–201 °C; ¹H NMR δ 12.51 (s, 1H), 8.36 (d, *J* = 7.9 Hz, 1H), 8.26 (d, *J* = 7.8 Hz, 1H), 7.65 (dd, *J* = 13.0, 8.3 Hz, 2H), 7.50 (t, *J* = 7.4 Hz, 1H), 7.41 (t, *J* = 7.5 Hz, 1H), 7.29 (dd, *J* = 14.6, 7.3 Hz, 2H), 6.80 (s, 1H), 3.81 (m, 2H), 3.60 (t, *J* = 5.7 Hz, 2H), 1.89 (m, 2H); ¹³C NMR δ 153.5, 146.0, 141.1, 138.5, 128.5, 126.1, 124.3, 121.9, 121.8, 121.2, 120.8, 120.5, 114.4, 111.8, 102.9, 59.4, 38.6, 32.9. ESI-HRMS: *m/z* calcd. for C₁₈H₁₇N₃O [M-H]⁺ 290.1293. Found 290.1296.

5.2.11. N-((Tetrahydrofuran-2-yl)methyl)-11H-indolo[3,2-c]quinolin-6-amine(**5k**)

Yield: 42%, Mp: 185–187 °C; ¹H NMR δ 12.48 (s, 1H), 8.30 (m, 1H), 8.25 (m, 1H), 7.67 (dd, *J* = 10.4, 5.0 Hz, 2H), 7.50 (t, *J* = 7.5 Hz, 1H), 7.42 (t, *J* = 7.6 Hz, 1H), 7.29 (dt, *J* = 17.5, 7.5 Hz, 2H), 6.49 (t, *J* = 5.3 Hz, 1H), 4.30 (m, 1H), 3.86 (m, 1H), 3.77 (dd, *J* = 7.8, 3.5 Hz, 2H), 3.66 (d, *J* = 7.3 Hz, 1H), 1.93 (m, 2H), 1.79 (m, 2H); ¹³C NMR δ 153.3, 146.4, 141.2, 138.6, 129.0, 126.64, 124.7, 122.0, 121.8, 121.3, 120.9, 120.6, 114.6, 111.9, 103.0, 77.6, 67.6, 44.9, 29.1, 25.6. ESI-HRMS: *m/z* calcd. for C₂₀H₁₉N₃O [M-H]⁺ 316.1450. Found 316.1444.

5.2.12. 4-(11H-Indolo[3,2-c]quinolin-6-yl)morpholine(**5l**)

Yield: 67%, Mp: >234 °C decompose; ¹H NMR δ 12.69 (s, 1H), 8.41 (d, *J* = 7.9 Hz, 1H), 7.94 (d, *J* = 7.9 Hz, 1H), 7.88 (d, *J* = 8.3 Hz, 1H), 7.71 (d, *J* = 8.1 Hz, 1H), 7.62 (s, 1H), 7.50 (t, *J* = 7.5 Hz, 1H), 7.46 (t, *J* = 7.6 Hz, 1H), 7.36 (d, *J* = 7.5 Hz, 1H), 3.99–3.91 (m, 4H), 3.45 (s, 4H); ¹³C NMR δ 153.6, 145.1, 140.1, 138.6, 128.4, 128.3, 124.8, 124.68, 121.7, 121.2, 121.1, 120.7, 115.4, 112.0, 103.6, 40.5(2C), 32.8(2C). Anal. calcd for C₁₉H₁₇N₃O: C 75.23, H 5.65, N 13.85. Found: C 75.15, H 5.28, N 13.62.

5.2.13. N-Benzyl-11H-indolo[3,2-c]quinolin-6-amine (**5m**)

Yield: 48%, Mp: 205–207 °C; ¹H NMR δ 12.51 (s, 1H), 8.53 (d, *J* = 7.9 Hz, 1H), 8.29 (d, *J* = 8.0 Hz, 1H), 7.69 (d, *J* = 8.1 Hz, 1H), 7.66 (d, *J* = 8.3 Hz, 1H), 7.52 (d, *J* = 8.0 Hz, 2H), 7.44 (t, *J* = 7.6 Hz, 1H), 7.33–7.26 (m, 5H), 7.18 (t, *J* = 7.0 Hz, 1H), 5.01

(d, J = 5.8 Hz, 2H); ^{13}C NMR δ 153.0, 146.4, 142.0, 141.4, 138.6, 128.5 (3C), 127.9 (2C), 126.8, 126.7, 124.4, 122.0, 121.9, 121.3, 121.2, 120.6, 114.7, 111.9, 103.1, 44.0. ESI-HRMS: m/z calcd. for $\text{C}_{22}\text{H}_{17}\text{N}_3[\text{M}-\text{H}]^+$ 322.1344. Found 322.1336.

5.2.14. *N*-Phenyl-11*H*-indolo[3,2-*c*]quinolin-6-amine (**5n**)

Yield: 73%; ^1H NMR δ 12.54 (m, 1H), 8.60 (d, J = 7.8 Hz, 1H), 8.35 (d, J = 8.0 Hz, 1H), 7.94 (d, J = 8.2 Hz, 1H), 7.79 (d, J = 8.1 Hz, 1H), 7.71 (dd, J = 13.5, 6.9 Hz, 3H), 7.58 (s, 1H), 7.50 (dt, J = 21.3, 7.6 Hz, 3H), 7.36 (t, J = 7.6 Hz, 1H), 7.31–7.25 (m, 1H); ^{13}C NMR δ 149.2, 143.0, 139.2(2C), 130.5, 129.8(2C), 129.3, 128.6, 125.9, 125.7, 124.8, 123.1, 122.2(2C), 121.8, 121.6(2C), 114.3, 112.7, 103.0.

5.2.15. *N*-(2,4-Dimethoxyphenyl)-11*H*-indolo[3,2-*c*]quinolin-6-amine (**5o**)

Yield: 96%, Mp: 220–221 °C; ^1H NMR δ 12.70 (s, 1H), 8.94 (d, J = 8.8 Hz, 1H), 8.34 (d, J = 7.6 Hz, 1H), 8.16 (d, J = 7.9 Hz, 1H), 7.97 (s, 1H), 7.81 (d, J = 8.3 Hz, 1H), 7.75 (d, J = 8.0 Hz, 1H), 7.59 (dd, J = 11.1, 4.0 Hz, 1H), 7.50 (t, J = 7.5 Hz, 1H), 7.44 (t, J = 7.4 Hz, 1H), 7.40 (t, J = 7.4 Hz, 1H), 6.76 (d, J = 2.6 Hz, 1H), 6.65 (dd, J = 8.8, 2.6 Hz, 1H), 4.03 (s, 3H), 3.79 (s, 3H); ^{13}C NMR δ 155.1, 150.5, 149.7, 145.8, 141.4, 138.8, 128.9, 127.3, 124.9, 124.1, 122.6, 122.1, 121.4, 121.2, 120.5, 119.6, 115.1, 112.6, 104.6, 103.6, 99.2, 56.8, 55.8. ESI-HRMS: m/z calcd. for $\text{C}_{23}\text{H}_{19}\text{N}_3\text{O}$ [M-H]⁺ 368.1399. Found 368.1398.

5.2.16. *N*^{*l*}-(2-Fluoro-11*H*-indolo[3,2-*c*]quinolin-6-yl)propane-1,3-diamine (**5p**)

Yield: 87%; ^1H NMR δ 8.42 (d, J = 8.0 Hz, 1H), 8.01 (dd, J = 9.6, 3.0 Hz, 1H), 7.65 (dd, J = 9.0, 5.3 Hz, 2H), 7.442 (m, 1H), 7.36 (m, 1H), 7.33 (m, 1H), 7.07 (s, 1H), 3.76 (d, J = 5.2 Hz, 2H), 2.73 (t, J = 6.2 Hz, 2H), 1.81 (m, 2H); ^{13}C NMR δ 156.2 (J = 237.1 Hz), 153.0, 143.4, 140.6 (d, J = 3.6 Hz), 138.5, 128.5 (d, J = 8.4 Hz), 124.6, 121.7, 121.2, 120.7, 116.8 (d, J = 24.1 Hz), 114.4 (d, J = 9.6 Hz), 111.9, 106.2 (d, J = 23.1 Hz), 103.6, 40.5, 39.7, 32.9. ESI-HRMS: m/z calcd. for $\text{C}_{18}\text{H}_{17}\text{FN}_4[\text{M}-\text{H}]^+$ 307.1359. Found 307.1364.

5.2.17. *N^l-(1-Bromo-1H-indolo[3,2-c]quinolin-6-yl)propane-1,3-diamine(5q)*

Yield: 79%, Mp: 117–119°C; ¹H NMR δ 11.78 (s, 1H), 8.47 (d, *J*= 8.0 Hz, 1H), 7.98 (d, *J*= 8.1 Hz, 1H), 7.68 (d, *J*= 8.3 Hz, 1H), 7.49 (dd, *J*= 7.5, 0.9 Hz, 1H), 7.45 (t, *J*= 7.6 Hz, 1H), 7.37 (t, *J*= 7.9 Hz, 1H), 7.32 (dd, *J*= 13.0, 5.8 Hz, 2H), 3.84 – 3.74 (m, 2H), 2.74 (t, *J*= 6.1 Hz, 2H), 1.87–1.77 (m, 2H); ¹³C NMR δ 153.5, 148.5, 138.7, 138.5, 128.7, 126.9, 126.2, 124.8, 121.1, 120.8, 120.7, 115.9, 114.0, 113.4, 104.7, 40.5, 39.8, 32.8. ESI-HRMS: *m/z* calcd. for C₁₈H₁₇BrN₄[M-H]⁺ 367.0560. Found 367.0558.

5.2.18. *N^l-(2-Bromo-1H-indolo[3,2-c]quinolin-6-yl)propane-1,3-diamine (5r)*

Yield: 82%, Mp: 181–183°C; ¹H NMR δ 8.50 (s, 1H), 8.44 (d, *J*= 8.0 Hz, 1H), 7.66 (d, *J*= 8.1 Hz, 1H), 7.58 (m, 2H), 7.42 (t, *J*= 7.5 Hz, 1H), 7.30 (t, *J*= 7.5 Hz, 1H), 7.25 (s, 1H), 3.79 (s, 2H), 2.75 (t, *J*= 6.1 Hz, 2H), 1.81 (m, 2H); ¹³C NMR δ 153.7, 145.3, 140.0, 138.6, 1301.0, 128.640, 124.7, 124.2, 121.6, 121.2, 120.78, 116.1, 112.8, 112.0, 103.6, 40.5, 39.7, 32.8.

5.2.19. *N^l-(2-Methyl-1H-indolo[3,2-c]quinolin-6-yl)propane-1,3-diamine(5s)*

Yield: 61%, Mp: 229–231°C; ¹H NMR δ 8.38 (d, *J*= 7.8 Hz, 1H), 8.03 (s, 1H), 7.62 (d, *J*= 8.0 Hz, 1H), 7.55 (d, *J*= 8.4 Hz, 1H), 7.38 (t, *J*= 7.4 Hz, 1H), 7.31 (d, *J*= 8.2 Hz, 1H), 7.26 (t, *J*= 7.4 Hz, 1H), 3.76 (d, *J*= 5.8 Hz, 2H), 2.73 (t, *J*= 5.6 Hz, 2H), 2.46 (s, 3H), 1.84–1.76 (m, 2H); ¹³C NMR δ 153.1, 144.8, 141.0, 138.6, 130.1, 129.9, 126.5, 124.2, 122.0, 121.4, 121.1, 120.5, 114.4, 111.9, 103.24, 40.5, 39.7, 33.0, 21.5. ESI-HRMS: *m/z* calcd. for C₁₉H₂₁N₄[M+H]⁺ 305.1766. Found 305.1745.

5.2.20. *N^l-(2-Methoxy-1H-indolo[3,2-c]quinolin-6-yl)propane-1,3-diamine(5t)*

Yield: 81%, Mp: 93–95°C; ¹H NMR δ 8.40 (d, *J*= 7.9 Hz, 1H), 7.79 (d, *J*= 2.8 Hz, 1H), 7.66 (d, *J*= 8.0 Hz, 1H), 7.59 (d, *J*= 9.0 Hz, 1H), 7.40 (t, *J*= 7.5 Hz, 1H), 7.27 (t, *J*= 7.5 Hz, 1H), 7.14 (dd, *J*= 9.0, 2.8 Hz, 1H), 3.89 (s, 3H), 3.76 (t, *J*= 6.4 Hz, 2H), 2.75 (t, *J*= 6.2 Hz, 2H), 1.82 (dd, *J*= 12.5, 6.2 Hz, 2H); ¹³C NMR δ 154.1, 152.2, 141.5, 141.0, 138.5, 127.9, 124.3, 122.0, 121.1, 120.4, 118.8, 114.5, 111.8, 103.4, 102.6, 55.8,

40.4, 39.6, 32.9.

5.2.21. *N^l-(2-Nitro-11H-indolo[3,2-c]quinolin-6-yl)propane-1,3-diamine (5u)*

Yield: 87%, Mp: >230 °C decompose; ¹H NMR δ 9.32 (s, 1H), 8.48 (d, *J*= 7.9 Hz, 1H), 8.23 (d, *J*= 9.2 Hz, 1H), 7.69 (t, *J*= 7.6 Hz, 2H), 7.46 (t, *J*= 7.5 Hz, 1H), 7.33 (t, *J*= 7.5 Hz, 1H), 3.84 (t, *J*= 5.8 Hz, 2H), 2.75 (t, *J*= 5.9 Hz, 2H), 1.86–1.79 (m, 2H); ¹³C NMR δ 155.4, 150.5, 141.1, 140.4, 138.6, 126.9, 125.1, 122.6, 121.4, 121.2, 121.2, 119.5, 113.4, 112.3, 103.5, 39.3, 39.2, 31.1.

5.2.22. *N^l-(2-Chloro-11H-indolo[3,2-c]quinolin-6-yl)propane-1,3-diamine (5v)*

Yield: 95%, Mp: >230 °C decompose; ¹H NMR δ 8.45 (d, *J*= 8.0 Hz, 1H), 8.35 (d, *J*= 2.2 Hz, 1H), 7.65 (dd, *J*= 15.5, 8.5 Hz, 2H), 7.48–7.40 (m, 2H), 7.30 (t, *J*= 7.5 Hz, 1H), 7.24 (s, 1H), 3.79 (d, *J*= 4.2 Hz, 2H), 2.75 (t, *J*= 6.1 Hz, 2H), 1.81 (t, *J*= 6.2 Hz, 2H); ¹³C NMR δ 153.6, 145.1, 140.1, 138.6, 128.4, 128.3, 124.8, 124.7, 121.7, 121.2, 121.1, 120.8, 115.4, 112.0, 103.6, 40.5, 39.8, 32.9. ESI-HRMS: *m/z* calcd. for C₁₈H₁₈ClN₄[M+H]⁺ 325.1220. Found 325.1192.

5.2.23.

N^l-(2-Chloro-11H-indolo[3,2-c]quinolin-6-yl)-2-methylpropane-1,3-diamine (5w)

Yield: 97%, Mp: 214–216 °C; ¹H NMR δ 8.42 (d, *J*= 8.0 Hz, 1H), 8.32 (d, *J*= 2.5 Hz, 1H), 7.65 (d, *J*= 8.1 Hz, 1H), 7.62 (d, *J*= 8.8 Hz, 1H), 7.55 (s, 1H), 7.45 (dd, *J*= 8.8, 2.5 Hz, 1H), 7.44–7.40 (m, 1H), 7.32–7.25 (m, 1H), 3.77 (dd, *J*= 7.7, 5.3 Hz, 1H), 3.54 (dd, *J*= 8.5, 4.1 Hz, 1H), 2.71 (dd, *J*= 12.4, 4.6 Hz, 1H), 2.59 (dd, *J*= 12.4, 7.0 Hz, 1H), 1.98 (t, *J*= 3.9 Hz, 1H), 0.97 (d, *J*= 6.9 Hz, 3H); ¹³C NMR δ 153.6, 145.1, 140.1, 138.6, 128.4, 128.3, 124.8, 124.7, 121.67, 121.1, 121.1, 120.8, 115.3, 112.0, 103.6, 47.4, 46.5, 35.6, 17.0. ESI-HRMS: *m/z* calcd. for C₁₉H₂₀ClN₄[M+H]⁺ 339.1376. Found 339.1352.

5.2.24.

N^l-(2-Chloro-11H-indolo[3,2-c]quinolin-6-yl)-2,2-dimethylpropane-1,3-diamine (5x)

Yield: 71%, Mp: 226–228°C; ^1H NMR δ 8.38 (d, J = 7.9 Hz, 1H), 8.38 (m, 1H), 7.81 (s, 1H), 7.66 (d, J = 8.1 Hz, 1H), 7.62 (d, J = 8.9 Hz, 1H), 7.47–7.40 (m, 2H), 7.30 (t, J = 7.5 Hz, 1H), 3.63 (s, 2H), 2.55 (s, 2H), 0.99 (s, 6H); ^{13}C NMR δ 153.9, 145.1, 140.1, 138.7, 128.5, 128.2, 124.9, 124.8, 121.7, 121.2, 121.1, 121.0, 115.4, 112.1, 103.7, 51.9, 50.6, 24.7, 14.6 (2C). ESI-HRMS: m/z calcd. for $\text{C}_{20}\text{H}_{22}\text{ClN}_4[\text{M}+\text{H}]^+$ 353.1533 Found 353.1518.

5.3.1. N^1 -(11-Methyl-11H-indolo[3,2-c]quinolin-6-yl)propane-1,3-diamine (**7a**)

Yield: 62%; ^1H NMR δ 8.52 (d, J = 8.2 Hz, 1H), 8.45 (d, J = 7.9 Hz, 1H), 7.81 (d, J = 8.2 Hz, 1H), 7.71 (d, J = 8.2 Hz, 1H), 7.51 (t, J = 7.5 Hz, 1H), 7.47 (t, J = 7.7 Hz, 1H), 7.33 (t, J = 7.5 Hz, 1H), 7.27 (t, J = 7.5 Hz, 1H), 7.05 (s, 1H), 4.33 (d, J = 9.1 Hz, 3H), 3.79 (d, J = 5.6 Hz, 2H), 2.74 (t, J = 6.0 Hz, 2H), 1.82 (dd, J = 12.2, 6.0 Hz, 2H); ^{13}C NMR δ 153.2, 147.5, 140.6, 140.0, 128.2, 127.2, 124.4, 122.8, 121.1, 121.0, 120.9, 120.7, 115.1, 110.3, 103.4, 40.4, 39.7, 33.9, 32.9.

5.3.2.

2,2-Dimethyl- N^1 -(11-methyl-11H-indolo[3,2-c]quinolin-6-yl)propane-1,3-diamine (**7b**)

Yield: 52%, Mp: 127–129°C; ^1H NMR δ 8.52 (d, J = 8.3 Hz, 1H), 8.42 (d, J = 7.9 Hz, 1H), 7.82 (d, J = 8.3 Hz, 1H), 7.69 (d, J = 8.3 Hz, 1H), 7.61 (s, 1H), 7.54–7.44 (m, 2H), 7.34 (t, J = 7.5 Hz, 1H), 7.27 (dd, J = 8.1, 7.0 Hz, 1H), 4.34 (s, 3H), 3.64 (s, 2H), 2.53 (s, 2H), 0.99 (s, 6H); ^{13}C NMR δ 153.4, 147.4, 140.5, 140.0, 128.1, 127.0, 124.4, 122.8, 121.0, 121.0, 120.8, 120.7, 115.1, 110.3, 103.4, 51.9, 50.4, 35.9, 33.9, 24.7 (2C).

5.3.3.

N^1,N^1 -Dimethyl- N^3 -(11-methyl-11H-indolo[3,2-c]quinolin-6-yl)propane-1,3-diamine (**7c**)

Yield 82%, Mp: 158–160°C; ^1H NMR δ 8.53 (d, J = 8.3 Hz, 1H), 8.30 (d, J = 7.9 Hz, 1H), 7.83 (d, J = 8.3 Hz, 1H), 7.71 (d, J = 8.3 Hz, 1H), 7.52 (d, J = 0.9 Hz, 1H), 7.47 (d,

$J=7.3$ Hz, 1H), 7.37 (d, $J=7.8$ Hz, 1H), 7.28 (s, 1H), 7.15 (s, 1H), 4.35 (s, 3H), 3.75 (d, $J=5.6$ Hz, 2H), 2.46 (t, $J=6.3$ Hz, 2H), 2.25 (s, 6H), 1.88 (m, 2H); ^{13}C NMR δ 153.1, 147.5, 140.5, 139.9, 128.1, 127.3, 124.4, 122.8, 121.1, 120.9, 120.7, 120.4, 115.1, 110.4, 103.4, 58.9, 45.8 (2C), 41.1, 33.9, 26.6.

5.3.4.

N^l, N^l -Diethyl- N^l -(11-methyl-11H-indolo[3,2-c]quinolin-6-yl)pentane-1,4-diamine (7d)

Yield: 61%; ^1H NMR δ 8.50 (d, $J=8.3$ Hz, 1H), 8.38 (d, $J=7.9$ Hz, 1H), 7.78 (d, $J=8.3$ Hz, 1H), 7.73 (d, $J=8.3$ Hz, 1H), 7.51 (dd, $J=8.2, 7.0$ Hz, 1H), 7.47 (t, $J=7.7$ Hz, 1H), 7.34 (t, $J=7.5$ Hz, 1H), 7.26 (t, $J=7.6$ Hz, 1H), 5.98 (d, $J=8.3$ Hz, 1H), 4.31 (s, 3H), 2.40–2.33 (m, 6H), 1.85–1.78 (m, 1H), 1.67–1.60 (m, 1H), 1.51 (td, $J=13.7, 6.8$ Hz, 2H), 1.35 (d, $J=6.5$ Hz, 3H), 0.85 (d, $J=7.1$ Hz, 6H); ^{13}C NMR δ 153.0, 147.5, 140.7, 139.9, 128.0, 127.3, 124.4, 122.6, 121.1, 121.1, 120.8, 120.7, 115.1, 110.2, 103.4, 52.7, 46.7(2C), 45.8, 34.7, 33.8, 24.2, 21.5, 12.1(2C).

5.3.5. 11-Methyl-6-(4-methyl-1,4-diazepan-1-yl)-11H-indolo[3,2-c]quinoline (7e)

Yield: 55%; ^1H NMR δ 8.61 (d, $J=8.3$ Hz, 1H), 8.06 (d, $J=7.9$ Hz, 1H), 7.83–7.80 (dd, $J=19.8, 8.3$ Hz, 2H), 7.59 (dd, $J=8.2, 7.0$ Hz, 1H), 7.48 (dd, $J=8.1, 7.2$ Hz, 1H), 7.41 (dd, $J=8.1, 7.1$ Hz, 1H), 7.35 (t, $J=7.5$ Hz, 1H), 4.34 (s, 3H), 3.86–3.84 (m, 2H), 3.80–3.78 (m, 2H), 2.67–2.63 (m, 4H), 2.27 (s, 3H), 1.95–1.91 (m, 2H); ^{13}C NMR δ 157.5, 146.0, 142.0, 140.2, 128.4, 128.3, 124.8, 123.0, 122.8, 122.3, 121.0, 120.8, 116.3, 110.4, 106.5, 58.6, 56.9, 52.2, 51.1, 47.0, 33.9, 27.5.

5.3.6.

N^l -(2-Chloro-11-methyl-11H-indolo[3,2-c]quinolin-6-yl)propane-1,3-diamine(7f)

Yield: 67%, Mp: 171–173°C; ^1H NMR δ 8.46 (d, $J=7.9$ Hz, 1H), 8.43 (s, 1H), 7.81 (d, $J=8.3$ Hz, 1H), 7.68 (d, $J=8.8$ Hz, 1H), 7.49 (m, 2H), 7.34 (t, $J=7.4$ Hz, 1H), 7.20 (s, 1H), 4.31 (s, 3H), 3.78 (d, $J=5.3$ Hz, 2H), 2.74 (t, $J=6.1$ Hz, 2H), 1.81 (m, 2H); ^{13}C NMR δ 153.4, 146.0, 140.0, 139.5, 128.9, 128.2, 124.9, 124.8, 121.7, 121.2,

121.1, 120.4, 115.8, 110.5, 103.8, 40.6, 39.7, 33.6, 32.8.

5.3.7.

N¹-(2-Chloro-11-methyl-11H-indolo[3,2-c]quinolin-6-yl)-2,2-dimethylpropane-1,3-diamine(7g)

Yield: 67%, Mp: 180–182°C; ¹H NMR δ 8.46 (d, *J* = 2.3 Hz, 1H), 8.44 (d, *J* = 7.9 Hz, 1H), 7.86 (d, *J* = 8.4 Hz, 1H), 7.68 (d, *J* = 8.9 Hz, 1H), 7.51 (dd, *J* = 6.5, 2.4 Hz, 2H), 7.35 (s, 1H), 4.35 (s, 3H), 3.62 (d, *J* = 4.4 Hz, 2H), 2.54 (s, 2H), 0.99 (s, 6H); ¹³C NMR δ 153.6, 146.0, 140.1, 139.4, 128.7, 128.2, 124.8, 124.8, 121.7, 121.3, 120.9, 120.5, 115.8, 110.5, 103.9, 52.1, 50.7, 35.5, 33.6, 24.7 (2C).

5.3.8.

N¹-(2-Chloro-11-methyl-11H-indolo[3,2-c]quinolin-6-yl)-N³,N³-dimethylpropane-1,3-diamine(7h)

Yield: 61%, Mp: 119–121°C; ¹H NMR δ 8.42 (d, *J* = 2.3 Hz, 1H), 8.29 (d, *J* = 8.0 Hz, 1H), 7.82 (d, *J* = 8.3 Hz, 1H), 7.68 (d, *J* = 8.9 Hz, 1H), 7.49 (dd, *J* = 8.9, 2.4 Hz, 2H), 7.37 (s, 1H), 7.26 (s, 1H), 4.31 (s, 3H), 3.73 (d, *J* = 5.2 Hz, 2H), 2.45 (t, *J* = 6.3 Hz, 2H), 2.24 (s, 6H), 1.90–1.83 (m, 2H); ¹³C NMR δ 153.3, 146.0, 140.0, 139.4, 128.9, 128.2, 124.9, 124.8, 121.7, 121.1, 120.5, 120.4, 115.7, 110.5, 103.8, 58.8, 45.8 (2C), 41.1, 33.6, 26.5.

5.3.9.

N⁴-(2-Chloro-11-methyl-11H-indolo[3,2-c]quinolin-6-yl)-N¹,N¹-diethylpentane-1,4-diamine(7i)

Yield: 54%. ¹H NMR δ 8.46 (d, *J* = 2.3 Hz, 1H), 8.41 (d, *J* = 8.0 Hz, 1H), 7.84 (d, *J* = 8.3 Hz, 1H), 7.68 (d, *J* = 8.9 Hz, 1H), 7.53–7.48 (m, 2H), 7.36 (t, *J* = 7.5 Hz, 1H), 6.13 (d, *J* = 8.5 Hz, 1H), 4.67 (s, 1H), 4.34 (s, 3H), 2.47 (s, 6H), 1.81 (s, 1H), 1.63 (d, *J* = 6.5 Hz, 1H), 1.53 (d, *J* = 8.4 Hz, 2H), 1.33 (d, *J* = 6.5 Hz, 3H), 0.89 (t, *J* = 7.1 Hz, 6H); ¹³C NMR δ 153.2, 145.9, 140.0, 139.6, 128.9, 128.2, 124.9, 124.9, 121.7, 121.3, 121.0, 120.3, 115.7, 110.4, 103.8, 52.5, 46.7 (2C), 45.8, 34.4, 33.6, 23.8, 21.5 (2C), 11.7.

5.3.10. *N¹-(2-Bromo-11-methyl-11H-indolo[3,2-c]quinolin-6-yl)propane-1,3-diamine (7j)*

Yield: 58%, Mp: 153–155°C; ¹H NMR δ 8.55 (s, 1H), 8.46 (d, *J* = 8.0 Hz, 1H), 7.81 (d, *J* = 8.2 Hz, 1H), 7.61 (t, *J* = 8.1 Hz, 2H), 7.48 (d, *J* = 7.7 Hz, 1H), 7.33 (t, *J* = 7.5 Hz, 1H), 7.21 (s, 1H), 4.30 (s, 3H), 3.77 (d, *J* = 3.9 Hz, 2H), 2.74 (t, *J* = 6.2 Hz, 2H), 1.81 (m, 2H); ¹³C NMR δ 153.4, 146.2, 140.0, 139.3, 130.8, 129.1, 124.8, 124.6, 121.1, 121.0, 120.3, 116.4, 112.9, 110.4, 103.7, 30.4, 39.8, 33.6, 32.6.

5.3.11.

N¹-(2-Bromo-11-methyl-11H-indolo[3,2-c]quinolin-6-yl)-2,2-dimethylpropane-1,3-diamine (7k)

Yield: 61%, Mp: 217–219°C; ¹H NMR δ 8.54 (s, 1H), 8.42 (d, *J* = 7.9 Hz, 1H), 7.81 (d, *J* = 8.3 Hz, 2H), 7.60 (d, *J* = 6.1 Hz, 2H), 7.49 (t, *J* = 7.7 Hz, 1H), 7.34 (t, *J* = 7.5 Hz, 1H), 4.30 (s, 3H), 3.62 (s, 2H), 2.55 (s, 2H), 0.99 (s, 6H); ¹³C NMR δ 153.6, 146.1, 140.0, 139.2, 130.8, 129.0, 124.7, 124.6, 121.2, 120.9, 120.4, 116.5, 112.8, 110.4, 103.8, 52.0, 50.6, 35.4, 33.6, 24.7 (2C).

5.3.12.

N¹-(2-Bromo-11-methyl-11H-indolo[3,2-c]quinolin-6-yl)-N³,N³-dimethylpropane-1,3-diamine (7l)

Yield: 53%, Mp: 132–134°C; ¹H NMR δ 8.56 (d, *J* = 1.7 Hz, 1H), 8.30 (d, *J* = 8.0 Hz, 1H), 7.83 (d, *J* = 8.3 Hz, 1H), 7.648 (m, 2H), 7.49 (d, *J* = 7.3 Hz, 1H), 7.38 (d, *J* = 7.9 Hz, 1H), 7.28 (s, 1H), 4.32 (s, 3H), 3.74 (d, *J* = 5.3 Hz, 2H), 2.46 (t, *J* = 6.3 Hz, 2H), 2.24 (s, 6H), 1.81 (m, 2H); ¹³C NMR δ 153.4, 146.3, 140.0, 139.3, 130.9, 129.3, 124.9, 124.7, 121.2, 120.6, 120.4, 116.5, 113.0, 110.6, 103.8, 58.9, 45.9 (2C), 41.15, 33.7, 26.5. Anal. calcd for C₂₁H₂₃BrN₄: C 61.32, H 5.64, N 13.62. Found: C 61.30, H 5.31, N 13.40.

5.3.13.

N^l-(2-Fluoro-11-methyl-11H-indolo[3,2-c]quinolin-6-yl)propane-1,3-diamine(7m)

Yield: 36%, Mp: 116–118°C; ¹H NMR δ 8.44 (d, *J*= 7.9 Hz, 1H), 8.18 (dd, *J*= 10.8, 2.4 Hz, 1H), 7.77 (t, *J*= 10.0 Hz, 1H), 7.70 (dd, *J*= 9.1, 5.8 Hz, 1H), 7.45 (dd, *J*= 16.9, 9.1 Hz, 1H), 7.36 (ddd, *J*= 10.7, 8.5, 2.6 Hz, 1H), 7.31 (t, *J*= 7.5 Hz, 1H), 4.29 (d, *J*= 9.8 Hz, 3H), 3.75 (t, *J*= 5.9 Hz, 2H), 2.74 (t, *J*= 6.1 Hz, 2H), 1.86–1.78 (m, 2H); ¹³C NMR δ 156.1 (d, *J*= 237.1 Hz), 152.8, 144.2, 140.0, 139.9 (d, *J*= 3.0 Hz), 128.8 (d, *J*= 9.1 Hz), 124.7, 121.2, 121.0, 120.4, 116.6 (d, *J*= 24.1 Hz), 114.6 (d, *J*= 10.6 Hz), 110.3, 107.3 (d, *J*= 24.2 Hz), 103.8, 40.0, 39.5, 33.4, 32.3.

5.3.14. N^l-(2,11-Dimethyl-11H-indolo[3,2-c]quinolin-6-yl)propane-1,3-diamin (7n)

Yield: 46%, Mp: 112–114°C; ¹H NMR δ 8.45 (d, *J*= 7.8 Hz, 1H), 8.32 (s, 1H), 7.82 (d, *J*= 8.3 Hz, 1H), 7.63 (d, *J*= 8.1 Hz, 1H), 7.48 (t, *J*= 7.6 Hz, 1H), 7.39–7.32 (m, 2H), 4.37 (s, 3H), 3.78 (t, *J*= 6.1 Hz, 2H), 2.75 (t, *J*= 5.8 Hz, 2H), 2.51 (s, 3H), 1.86–1.79 (m, 2H); ¹³C NMR δ 152.8, 145.5, 140.3, 139.9, 129.9, 129.7, 126.9, 124.3, 121.9, 121.0, 120.8, 120.7, 114.9, 110.1, 103.4, 39.1, 33.8, 31.9, 22.9, 21.5.

5.3.15.

N^l-(2-Methoxy-11-methyl-11H-indolo[3,2-c]quinolin-6-yl)propane-1,3-diamine(7o)

Yield: 53%, Mp: 79–81°C; ¹H NMR δ 8.43 (d, *J*= 7.9 Hz, 1H), 7.90 (s, 1H), 7.80 (m, 1H), 7.65 (d, *J*= 9.0 Hz, 1H), 7.47 (s, 1H), 7.31 (s, 1H), 7.20 (m, 1H), 6.87 (m, 1H), 4.36 (d, *J*= 4.3 Hz, 3H), 3.91 (s, 3H), 3.74 (s, 2H), 2.73 (t, *J*= 6.2 Hz, 2H), 1.81 (m, 2H); ¹³C NMR δ 153.8, 152.1, 142.5, 140.2, 140.0, 128.5, 124.4, 121.1, 120.8, 120.7, 118.0, 115.0, 110.2, 103.9, 103.8, 55.8, 40.5, 39.7, 33.6, 32.9.

5.3.16. N^l-(11-Methyl-2-nitro-11H-indolo[3,2-c]quinolin-6-yl)propane-1,3-diamine (7p)

Yield: 27%, Mp: >250°C; ¹H NMR δ 8.40 (m, 1H), 7.92 (m, 1H), 7.73 (d, *J*= 8.3 Hz, 1H), 7.69 (d, *J*= 2.3 Hz, 1H), 7.45 (s, 1H), 7.42 (s, 1H), 7.26 (s, 1H), 6.90 (m, 1H), 4.28 (s, 3H), 3.68 (m, 2H), 2.71 (m, 2H), 1.79 (m, 2H); ¹³C NMR δ 155.1, 155.0, 151.5, 140.2, 140.0, 127.5, 127.4, 125.3, 122.3, 121.6, 121.1, 120.2, 113.6,

110.8, 110.7, 40.9, 33.6, 30.3, 29.2.

5.4. General procedure for the synthesis of

1-(3-(11-methyl-11H-indolo[3,2-c]quinolin-6-ylamino)propyl)-3-phenylurea(8)

*N*¹-(11-Methyl-11H-indolo[3,2-c]quinolin-6-yl)propane-1,3-diamine (**7a**, 30 mg) and was completely dissolved in THF (1 mL), and then a solution of phneylisocyanate (1.2 equiv) and THF (1 mL) were added drop by drop under stirring at room temperature for 6 h. TLC monitoring was used to ensure the complete of reaction. After reaction was finished, the reaction mixture was evaporated to dryness. The crude product was purified by flash chromatography using *n*-hexane-AcOEt (1:1) as an eluent to yield pure products. Yield:72%, Mp: 218–220°C; ¹H NMR δ 8.56 (s, 1H), 8.54 (d, *J*= 8.3 Hz, 1H), 8.49 (d, *J*= 7.9 Hz, 1H), 7.83 (d, *J*= 8.3 Hz, 1H), 7.75 (d, *J*= 8.3 Hz, 1H), 7.50 (dd, *J*= 16.2, 8.2 Hz, 2H), 7.42 (d, *J*= 8.4 Hz, 2H), 7.34 (t, *J*= 7.5 Hz, 1H), 7.28 (t, *J*= 7.6 Hz, 1H), 7.22 (t, *J*= 7.7 Hz, 2H), 6.88 (t, *J*= 7.3 Hz, 1H), 6.74 (d, *J*= 5.6 Hz, 1H), 6.33 (d, *J*= 5.7 Hz, 1H), 4.36 (s, 3H), 3.77 (q, *J*= 6.3 Hz, 2H), 3.27 (dd, *J*= 12.5, 6.3 Hz, 2H), 1.88 (m, 2H); ¹³C NMR δ 1561, 153.2, 147.4, 141.1, 140.6, 134.0, 129.1 (2C), 128.1, 127.3, 124.4, 122.8, 121.4, 121.2, 121.0, 120.9, 120.7, 118.2 (2C), 115.1, 110.3, 103.4,38.1, 37.3, 33.9, 30.8.

5.4. Biological assays

5.4.1. Cell line

Established *in vitro*, human cell line: MV4-11 (leukemia), A549 (lung cancer), HCT116 (colon cancer) and normal mice fibroblast (BALB/3T3) was used. All lines were obtained from American Type Culture Collection (Rockville, Maryland, USA) and are being maintained at the Institute of Immunology and Experimental Therapy, Wroclaw, Poland.

MV4-11 cells were cultured in the RPMI 1640 (IIET, Poland) supplemented with 2 mM L-glutamine, 1.0 mM sodium pyruvate and 10% fetal bovine serum (all from Sigma-Aldrich, Germany), HCT 116 and A549 cells were cultured in the RPMI 1640+OptiMEM (50:50) medium (IIET, Poland) supplemented with 2 mM

L-glutamine and 5% fetal bovine serum (all from Sigma-Aldrich Germany), BALB/3T3 cells were cultured in Dulbecco medium (IIET, Poland) supplemented with 2 mM L-glutamine and 1.0 mM sodium pyruvate, 10% fetal bovine serum (all from Sigma-Aldrich, Germany). All culture medium was supplemented with 100 units/ml penicillin (Sigma-Aldrich, Germany), and 100 µg/ml streptomycin (Polfa Tarchomin S.A., Poland). All cell lines were grown at 37°C with 5% CO₂ humidified atmosphere.

5.4.2. Cytotoxicity assay *in vitro*

Test solutions of the compounds tested (1 mg/ml) were prepared by dissolving the substances in 100 µl of DMSO completed with 900 µl of tissue culture medium. Afterwards, the tested compounds were diluted in culture medium to reach the final concentrations of 10, 1, 0.1, 0.01 and 0.001 µg/ml.

Twenty four hours prior to the addition of the tested compounds, the cells were plated in 96-well plates (Sarstedt, Germany) at a density of 1×10^4 cells per well. The assay was performed after 72 h of exposure to varying concentrations of the tested agents. The *in vitro* cytotoxic effect of all agents was examined using the MTT (MV4-11) or SRB (A549, HCT116 and BALB/3T3) assay [36].

The results were calculated as an IC₅₀ (inhibitory concentration 50) – the dose of tested agent which is cytotoxic for 50% of the cancer cells. IC values were calculated for each experiment separately and mean values $\pm$ SD are presented in the Table 1, 2, 3 and 4. Each compound in each concentration was tested in triplicate in a single experiment, which was repeated 3--5 times.

5.4.3. MTT assay

This technique was applied for the cytotoxicity screening against leukemia cells growing in suspension culture. An assay was performed after 72-hours exposure to varying concentrations (from 0.001 to 10 µg/ml) of the tested agents. For the last 3-4 hours of incubation 20 µl of MTT solution were added to each well (MTT: 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyl tetrazolium bromide; stock solution: 5

mg/ml, Sigma-Aldrich, Germany). The mitochondria of viable cells reduce the pale yellow MTT to a navy blue formazan: the more viable cells are present in well, the more MTT will be reduced to formazan. When incubation time was completed, 80 μ l of the lysing mixture were added to each well (lysing mixture: 225 ml dimethylformamide, POCh, Gliwice, Poland, 67.5 g sodium dodecyl sulphate, Sigma-Aldrich, Germany, and 275 ml of distilled water). After 24 h, when formazan crystals had been dissolved, the optical densities of the samples were read on Synergy H4 photometer (BioTek Instruments, USA) at 570 nm wavelength.

5.4.4. SRB assay

This technique was applied for the cytotoxicity screening against cells growing in adherent culture. The details of this technique were described by Skehan [37]. The cytotoxicity assay was performed after 72-hour exposure of the cultured cells to varying concentrations (from 0.01 to 10 μ g/ml) of the tested agents. The cells attached to the plastic were fixed by gently layering cold 50% TCA (trichloroacetic acid, Aldrich-Chemie, Germany) on the top of the culture medium in each well. The plates were incubated at 4 °C for 1 h and then washed five times with tap water. The background optical density was measured in the wells filled with culture medium, without the cells. The cellular material fixed with TCA was stained with 0.1% sulforhodamine B (SRB, Sigma, Germany) dissolved in 1% acetic acid (POCh, Gliwice, Poland) for 30 minutes. Unbound dye was removed by rinsing (4x) with 1% acetic acid. The protein-bound dye was extracted with 10 mM unbuffered Tris base (Sigma, Germany) for determination of optical density (at 540 nm) on Synergy H4 photometer (BioTek Instruments, USA).

5.4.5. DNA binding ability of 5g and 7h

The salmon fish sperm DNA was used directly without further purification. A phosphate buffer (pH 7.0) was used to control the pH of reaction system and the sample was dissolved in phosphate buffer with 2.5% DMSO. Solutions in buffer were

freshly prepared immediately before being used. The UV absorption spectra were recorded with Hitachi U-2910 spectrophotometer in a 1 cm path length quartz cuvette at indicated wavelength.

Measurements were carried out at 20 °C. In absorption experiments, the concentration of the compound **5g** (or **7h**) was maintained ($C = 50 \mu\text{mol/L}$) and different amount of DNA were added ($C_{DNA} = 0.00, 0.01, 0.02, 0.03, 0.04, 0.05, 0.06, 0.07, 0.08, 0.09, 0.10, 0.11, 0.12, 0.13, 0.14, 0.15, 0.16, 0.17, 0.18, 0.19, 0.20, 0.21, 0.22 \mu\text{mol/L}$). The binding constant K between compound and DNA was calculated from the ratio of the slop to the intercept of the linear plot.

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Scheme 1. Synthesis of 11H- and 11Me-indolo[3,2-*c*]quinolines with amino group substituted at the C-6 position. Reagents and conditions: (i) AcOH, reflux, 8–20 h; (ii) POCl₃, 130 °C, 8 h; (iii) appropriate amines, 90–140 °C, 20 min–4 h; (iv) MeI, NaH, 0 °C–RT, 4 h; (v) appropriate amines, 140 °C, 24 h or with MW at 140 °C, 4 h; (vi) PhNCO, THF, RT.

Cryptolepine (i)

Neocryptolepine (ii)

Isocryptolepine (iii)

11H-Indolo[4,3-c]quinolines **iv** (R = H)
11Me-Indolo[4,3-c]quinolines **v** (R = Me)

Fig. 1. Structures of indoloquinolines from *Cryptolepis sanguinolenta* and their derivatives.

Fig. 2. (a) UV-vis absorption spectra of compound **7h** and **7h**-DNA at 20 °C. $C_{7h} = 50$ $\mu\text{mol/L}$, $C_{\text{DNA}} = 0.00, 0.01, 0.02, 0.03, 0.04, 0.05, 0.06, 0.07, 0.08, 0.09, 0.10, 0.11, 0.12, 0.13, 0.14, 0.15, 0.16, 0.17, 0.18, 0.19, 0.20, 0.21, 0.22$ $\mu\text{mol/L}$ for curves 1-23 in pH 7.0 phosphate buffer solution; (b) The plot of $A_0/(A_0-A)$ vs $1/[\text{DNA}]$ for **7h**-DNA. (c) UV-vis absorption spectroscopy of compound **5g** and **5g**-DNA at 20 °C. $C_{5g} = 50$ $\mu\text{mol/L}$, $C_{\text{DNA}} = 0.00, 0.01, 0.02, 0.03, 0.04, 0.05, 0.06, 0.07, 0.08, 0.09, 0.10, 0.11, 0.12, 0.13, 0.14, 0.15, 0.16, 0.17, 0.18, 0.19, 0.20, 0.21, 0.22$ $\mu\text{mol/L}$ for curves 1-23 in pH 7.0 phosphate buffer solution; (d) The plot of $A_0/(A_0-A)$ vs $1/[\text{DNA}]$ for **5g**-DNA.

Table 1. Cytotoxic effect of 6-amino-11*H*-indolo[3,2-*c*]quinolines against human leukemia

MV4-11 cell line.

Compound	R ¹	R ²	MV4-11 IC ₅₀ (μM)
cisplatin			2.36±0.68
doxorubicin HCl			0.006±0.002
4a	H	Cl	9.14±2.45
5a	H		0.12±0.01
5b	H		0.70±0.19
5c	H		0.61±0.13
5d	H		0.71±0.01
5e	H		0.39±0.07
5f	H		0.85±0.26
5g	H		0.41±0.31
5h	H		0.74±0.31
5i	H		0.44±0.27
5j	H		0.38±0.21
5k	H		0.75±0.11
5l	H		9.43±2.70
5m	H		0.77±0.22
5n	H		8.37±2.20
5o	H		7.28±1.14

5p	2-F		0.59±0.19
5q	1-Br		0.60±0.22
5r	2-Br		0.65±0.14
5s	2-Me		0.14±0.04
5t	2-MeO		0.12±0.05
5u	2-NO ₂		0.15±0.06
5v	2-Cl		0.56±0.17
5w	2-Cl		0.62±0.05
5x	2-Cl		0.59±0.08

Table 2. Cytotoxic effect of 6-amino-11*H*-indolo[3,2-*c*]quinolines against normal mice fibroblast BALB/3T3 and against cancer cell lines A549 and HCT116.

No.	BALB/3T3	A549	HCT116
	IC ₅₀ (μM)	IC ₅₀ (μM)	IC ₅₀ (μM)
cisplatin	8.53±3.53	7.83±2.60	3.47±0.77
doxorubicinHCl	1.08±0.03	0.33±0.10	0.39±0.10
5a	1.05±0.13	0.17±0.05	0.26±0.11
5b	1.14±0.09	1.16±0.09	1.06±0.01
5c	1.01±0.05	1.05±0.03	1.06±0.14
5d	1.07±0.19	1.06±0.12	1.08±0.21
5e	1.15±0.34	0.76±0.14	0.98±0.12
5f	10.11±1.08	2.46±0.32	1.73±0.11
5g	1.18±0.20	0.87±0.27	0.55±0.17
5h	8.96±1.82	1.97±0.51	1.65±0.37
5i	0.83±0.07	1.45±0.33	0.19±0.02
5j	0.86±0.23	2.21±0.36	0.26±0.14
5k	3.04±0.85	1.40±0.13	1.28±0.31

5m	8.04±2.81	1.99±0.28	1.46±0.24
5s	0.92±0.23	0.21±0.00	0.08±0.02
5t	0.31±0.03	0.16±0.03	0.07±0.03
5u	0.36±0.15	0.35±0.22	0.10±0.02

Table 3. Cytotoxic effect of 6-amino-11-methyl-indolo[3,2-*c*]quinolines against human leukemia MV4-11 cell line.

Compound	R ¹	R ²	MV4-11 IC ₅₀ (μM)
cisplatin			2.36±0.68
doxorubicinHCl			0.006±0.002
6	H	Cl	16.57±2.96
7a	H		0.11±0.04
7b	H		0.15±0.05
7c	H		0.14±0.01
7d	H		0.07±0.03
7e	H		0.96±0.27
7f	2-Cl		0.12±0.06
7g	2-Cl		0.56±0.13
7h	2-Cl		0.08±0.03
7i	2-Cl		0.57±0.24
7j	2-Br		0.43±0.06
7k	2-Br		0.50±0.11
7l	2-Br		0.39±0.17
7m	2-F		0.17±0.07
7n	2-Me		0.09±0.03
7o	2-MeO		0.10±0.04
7p	2-NO ₂		0.05±0.01

Table 4. Cytotoxic effect of 6-amino-11-methyl-indolo[3,2-*c*]quinolines against normal mice fibroblast BALB/3T3 and against cancer cell lines A549 and HCT116.

No.	BALB/3T3	A549	HCT116
	IC ₅₀ (μM)	IC ₅₀ (μM)	IC ₅₀ (μM)
cisplatin	8.53±3.53	7.83±2.60	3.47±0.77
doxorubicinHCl	1.08±0.03	0.33±0.10	0.39±0.10
7a	0.95±0.24	0.18±0.03	0.06±0.02
7b	0.70±0.23	0.54±0.27	0.13±0.02
7c	0.78±0.28	0.14±0.05	0.20±0.06
7d	0.50±0.16	0.11±0.04	0.05 ±0.02
7f	0.94±0.06	0.73±0.18	0.11±0.02
7h	0.82±0.08	0.57±0.31	0.10±0.02
7m	0.98±0.07	0.25 ±0.05	0.11±0.01
7n	0.42±0.12	0.14±0.03	0.07±0.019
7o	0.10±0.02	0.11±0.06	0.01±0.00
7p	0.08±0.02	0.11±0.07	0.01±0.00
8	6.11±1.44	1.19±0.42	0.82±0.05

Synthesis and in vitro cytotoxic effect of 6-amino-substituted 11*H*- and 11Me-indolo[3,2-*c*]quinolines

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