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7-Deacetyl-10-alkylthiocolchicine derivatives – new compounds with potent anticancer and fungicidal activity†

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A series of new semi-synthetic 7-deacetyl-10-alkylthiocolchicine derivatives with ethyl, *n*-propyl, *i*-propyl and *n*-butyl substituents were synthesised and characterised by spectroscopic methods, elemental analysis, DFT calculations and molecular docking simulations. All the synthesized compounds have been tested for fungicidal and anticancer activities against SKOV-3, LoVo, MCF-7, MDA-MB-231 and the lung-derived fibroblast CCD39Lu. All the new colchicine derivatives exhibit significantly higher cytotoxicity towards the SKOV-3 tumour cell line than the natural product – colchicine. The most effective cytotoxic agents were 7-deacetyl-10-*n*-butylthiocolchicine and 7-deacetyl-10-*i*-propylthiocolchicine. Among all the compounds tested, 7-deacetyl-10-*n*-butylthiocolchicine exhibited the highest fungicidal activity. Molecular modeling indicated that several mutations found in the β -tubulin unit of the tested fungal strains are crucial for antifungal activity and selectivity of 7-deacetyl-10-*n*-butylthiocolchicine. The obtained results may be useful for the development of selective colchicine derivatives as effective fungicidal and/or anticancer drugs.

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Introduction

Colchicine (**1**, Fig. 1) is an alkaloid isolated from *Colchicum autumnale* and *Gloriosa superba* which is known to show notable anti-inflammatory, anti-mitotic, and anti-fibrotic effects.^{1,2} The colchicine behaviour in the human body, its anti-inflammatory and anticancer properties and its interaction with amino acids in tubulin have been studied for many years.^{3–5} Although colchicine shows significant *in vitro* anti-tumor effects, it has limited applications in medicine because of its high toxicity.⁶ One of the best known colchicine derivatives is 10-methylthiocolchicine (known as thiocolchicine) (**2**, Fig. 1 (ref. 7 and 8)) – a compound with higher biological ac-

tivity than colchicine **1** and with confirmed anti-cancer properties but is almost insoluble in water.^{9,10} Other 10-alkylthiocolchicine derivatives **3–6** with alkyl chains C2 to C4 ($-C_2H_5$, $n-C_3H_7$, $i-C_3H_7$ and $n-C_4H_9$) were also obtained and their cytotoxic activity was tested.⁸ Unfortunately, these

Fig. 1 Colchicine **1** and its derivatives **2–11**.

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compounds were less active than **2**.⁸ The insolubility of compound **2** in water limits the interest in this compound as a drug candidate. 10-Methylthiocolchicine, however, has so far been receiving scientific interest as a starting compound to obtain other biologically active derivatives.^{10–19} One of these is 7-deacetyl-10-methylthiocolchicine **7**, Fig. 1, the inhibitory effect of which has been tested on tubulin assembly.^{13,20–23} Both 10-methylthiocolchicine **2** and its derivative **7** have been screened as conjugate compounds for tubulin.²³ Many derivatives of **7** have been also obtained and tested as anticancer agents,^{14,15,17,24,25} e.g. thiocolchicoside (3-O-glycosyl-3-demethylthiocolchicine) is a muscle relaxing agent and an anti-inflammatory drug.²⁶ Despite the large number of known colchicine derivatives, there remains a need for new derivatives with better biological activity than the starting compound. Hence, in the present communication, we report the synthesis and characterization of new thiocolchicine analogues showing good water solubility and better fungicidal and anticancer activity than colchicine **1** and thiocolchicine **2**.

Results and discussion

The aim of the current studies is to determine the cytotoxic and fungicidal activity of new colchicine **1** derivatives. The synthesis of new alkylthiocolchicine derivatives **7–11** with $-\text{CH}_3$, $-\text{C}_2\text{H}_5$, $n\text{-C}_3\text{H}_7$, $i\text{-C}_3\text{H}_7$ and $n\text{-C}_4\text{H}_9$ substituents at the C-10 carbon atom is presented in Scheme 1. The experimental and full spectral data for compounds **7–11** are given in the ESI.† The obtained compounds were characterized by spectroscopic methods (¹³C NMR, ¹H NMR, FT-IR, EI-MS, UV-vis, and elemental analysis) as well as by DFT and molecular docking calculations.

The cytotoxic activity of all the 7-deacetyl-10-alkylthiocolchicines **7–11** against SKOV-3 (human cancer ovarian cells), LoVo (human colon carcinoma), estrogen-dependent MCF-7, estrogen-independent MDA-MB-231 breast cancer cells and the lung-derived fibroblast CCD39Lu and their antifungal activity against selected molds were also

studied. All the cell lines used in the experiments were obtained from The European Collection of Cell Cultures (ECACC) (Salisbury, UK) via Sigma-Aldrich, Poland. For the experiments, two types of cell cultures were used: proliferating and growth-arrested cells.

The UV-vis spectra of compounds **7–11** revealed bathochromic shifts with respect to the spectra of compounds **2–6**, which were explained by the disappearance of the acetyl substituent at the C-7 position in coupled trimethoxyphenyl and tropolonic chromophores, from 255–258 nm for **2–6** to 245–250 nm for **7–11** and from 385–388 to 360–375 nm for trimethoxyphenol and tropolonic chromophores, respectively. The ¹H and ¹³C NMR spectra of the 7-deacetyl-10-alkylthiocolchicine derivatives **7–11** were recorded in two different solvents: DMSO-*d*₆ and CDCl₃, the details are given in the ESI.† In the EI-MS mass spectra (see the ESI,† Fig. S2–S5†), all the new colchicine derivative signals of molecular ions are observed at $m/z = 372$ (for **7**), $m/z = 387$ (for **8**), $m/z = 401$ (for **9** and **10**) and $m/z = 415$ (for **11**). In the FT-IR spectra (KBr pellets), as a result of the deacetylation of the acetamide substituent at the C-7 position, the bands assigned to the stretching vibration of C=O for compounds **2–6** in the region 1681–1678 cm^{−1} disappeared (see the ESI,† Fig. S6–S10†). The second band assigned to the stretching vibration of C=O assigned to C-9 of the tropolone ring which appeared in the region of 1603–1606 cm^{−1} for **2–6** shifted to the lower wave numbers of 1598–1596 cm^{−1} for compounds **7–11**.

The natural (−)-(7*S*)-colchicine has two aromatic moieties arranged counterclockwise. Colchicine displays molecular asymmetry derived from a non-planar arrangement of the tropolonic ring C and trimethoxyphenyl ring A. Rings A and C are twisted around the C1a–C12a bond, the helicity around this bond is *aR* and the torsion angle is close to 53° in colchicine and its biologically active derivatives.²⁷ Additional information about colchicine and its derivatives **2–11** was obtained at the theoretical level. The geometry optimization in the gas phase of molecules **1–11** was performed using the DFT method B3LYP in combination with the 6-31G basis set using the Gaussian03 program package (see the ESI† p. S19). The calculated dihedral angles for compounds **2–5**, **7**, **8** and **11** are close to those for **1**.

The calculated energies of the optimized structures and the dihedral angles are presented in Table 1. The results clearly indicate that the thiocolchicines are the more stable compounds in the gas phase compared to colchicine. The data collected in Table 1 reveal that the calculated energy difference between compounds **2** and **7** is −190.593435 H and the difference in the computed energy between the thiocolchicine derivatives **3–6** and their deacetyl counterparts **8–11** are lower and almost the same (approx. −152 H) irrespective of the length of the thioalkyl chain at the C-10 position.

The new colchicine derivatives have been studied mainly as potential anticancer agents because of the antimetabolic properties of colchicine. The cytotoxic activity of 10-alkylthio analogues **7–11** was screened on the human ovarian cancer

Scheme 1 Synthesis of 10-alkylthiocolchicines^a and 7-deacetyl-10-alkylthiocolchicines^b. Reagents and conditions: ^acolchicine (**1**), RSNa (R: Me, Et, *i*Pr, *n*Pr, *n*Bu), water, ~40 °C for 2–14 h; ^b10-alkylthiocolchicine (**2–6**), HCl (aq)/MeOH, reflux at ~70 °C for 6–16 h. The time for completion of all the reactions was indicated by TLC.

Table 1 Calculated dihedral angles [1-1a-12a-12] and energies of colchicine **1** and its derivatives **2-11**. The total energies are given in hartrees ($H = 627.5 \text{ kcal mol}^{-1}$)

Compound	Energy	ΔEnergy^a	Dihedral angle
1	-1397.57135849	—	52.75057
2	-1680.05840199	-190.593435	53.64795
3	-1681.38806998	-152.619133	53.95637
4	-1720.69238336	-152.619024	53.66950
5	-1720.69364176	-152.619006	53.82392
6	-1759.99516748	-152.619676	54.01425
7	-1489.46496671	—	53.97105
8	-1528.76893614	—	53.71845
9	-1568.07335993	—	54.33612
10	-1568.07463599	—	54.39321
11	-1607.37549128	—	53.30232

^a Calculated as the difference between 10-alkylthiocolchicines (**2-6**) and 7-deacetyl-10-alkylthiocolchicines (**7-11**).

cell line SKOV-3, the human colon cancer cell line LoVo, two human breast cancer cell lines MCF-7 and MDA-MB-231 and the lung fibroblast CCD39Lu (Table 2). In the cytotoxicity studies, the tested compounds were dissolved in DMSO (final concentration: 0.1%) and as a positive control, doxorubicin was used, while as a negative control, DMSO alone was administered.

The IC_{50} values were calculated from the concentration-effect curves obtained in GraphPad Prism version 6.00 for Windows (GraphPad Software, La Jolla California, USA). Statistical analyses were carried out using one-way ANOVA

Table 2 The IC_{50}^a values (nM) of compounds **7-11** tested against selected cancer cell lines after 72 hours of incubation. Data were obtained from triplicate experiments. Doxorubicin was used as a positive control

Cell line	MCF-7	MDA-MB-231	DLD1	LoVo	CCD39Lu	
Doxorubicin	9.84	1240	145	78.3	850	
	IC ₅₀ [nM] proliferating cells					
	Compound					
Cell line	1	7	8	9	10	11
SKOV-3	198	1.3	305	22	4	9
MCF-7	41	670	1620	2080	4900	1460
MDA-MB-231	25	1260	3550	4240	5000	4180
DLD1	43	1180	510	3420	6260	720
LoVo	119	1020	390	3830	130	1870
CCD39Lu	586	1920	150	670	1680	2170

SKOV-3 cell line		
Compound	IC_{50} [nM] proliferating cells	IC_{50} [nM] non-proliferating cells
1	198	210*
7	1.3	9.6*
8	305	409*
9	22	46*
10	4	27*
11	9	62*
Doxorubicin	32.6	128

^a The compound concentration that inhibits tumor cell proliferation by 50%.

with Dunnett's multiple comparison tests. Moreover, the statistically significant differences ($p < 0.005$) between the values for proliferating and growth-arrested cells are marked with asterisks (for the SKOV-3 cell line). As we can see from Table 2, the cytotoxic activity of the tested compounds towards the SKOV-3 cell line was significantly higher than the activity of colchicine **1**. Surprisingly, except compound **7** (whose high activity was expected), the derivatives with longer alkylthio chains (**10** and **11**) showed high activity. Moreover, the tested compounds were significantly more highly active against proliferating cells when compared to growth-arrested cells which suggested their interaction with cellular mitotic mechanisms. Further studies are necessary in order to fully explain their antimitotic activity (Table 2).

Colchicine binding to fungal tubulins is characterized with lower affinity as compared with that to mammalian tubulins.²⁸ Colchicine has been tested previously for antifungal activity against some microfungi species.^{29,30} The results of the tests have shown that **1** inhibited the growth of *Candida*.³⁰ Colchicine significantly inhibited the fungicidal activity of neutrophils against *P. marneffei* in a dose-dependent manner and this inhibition was not due to its cytotoxic effect.³¹ Chronic human exposure to different microfungi species can cause symptoms of disease (*A. pullulans* can lead to hypersensitivity pneumonitis or "humidifier lung").^{32,33} In our previous study, colchicine complexes exhibited some fungicidal activity.³⁴ In this study, the fungicidal activity of new colchicine derivatives **7-11** as well as their 10-alkylthiocolchicines counterparts **2-6** was tested against eight fungal strains (screening test results are given in Table S2†). Two known fungicides, IPBC and chalcone, were tested as the reference. Amphotericin B ($1 \mu\text{g mL}^{-1}$) as a positive control and untreated agar medium as a negative control were used. The MIC and MFC values obtained for all the tested compounds are presented in Tables 3 and S2.† Colchicine **1** showed good activity against *A. pullulans* only but compounds **2-6** were completely inactive against all the tested microfungi species. The derivatives with longer alkylthio chains, 7-deacetyl-10-*n*-butylthiocolchicine **11** and 7-deacetyl-10-*n*-propylthiocolchicine **9**, were the most active compounds against **5** among the 8 tested fungi (Table 3). Among the compounds with a propylthio substituent, the one with the unbranched alkylthio chain **9** was less active than the one with an *i*-propylthio substituent **10**. Derivatives **9-11** were shown to be active against the following fungi strains: *P. variotii*, *P. funiculosum*, *T. viride*, and *P. cyclopium*, and **10** and **11** being especially active against *A. pullulans* and *Ch. globosum*. The results permit the conclusion that the antifungal properties of some new colchicine derivatives may be potentially useful for partly controlling strains.

Although lipophilicity as a property facilitating passive drug transport should increase the toxicity of the compounds tested, it is known that lipophilicity may also be a significant factor modulating molecular interactions resulting in changes in ligand-receptor binding or enzyme inhibition potency.³⁵ The calculated values of $\log P$ (Table 3) of the

Table 3 Antifungal activity of compounds **1–11** and the results of MIC and MFC [$\mu\text{g mL}^{-1}$ and mMol mL^{-1}] and lipophilicity

	MIC [$\mu\text{g mL}^{-1}$] and [mMol mL^{-1}] ^a								
	Fungi								
Compounds	<i>A. niger</i>	<i>A. versicolor</i>	<i>P. variotii</i>	<i>P. funiculosus</i>	<i>T. viride</i>	<i>P. cyclopium</i>	<i>A. pullulans</i>	<i>Ch. globosum</i>	Log P
1	>4000	>4000	>4000	>4000	>4000	>4000	1 $\pm$ 0.0 [2.5 $\times$ 10 ⁻¹²]	>4000	1.10
2	>4000	>4000	>4000	>4000	>4000	>4000	>4000	>4000	2.17
3	>4000	>4000	>4000	>4000	>4000	>4000	>4000	>4000	2.54
4	>4000	>4000	>4000	>4000	>4000	>4000	>4000	>4000	3.04
5	>4000	>4000	>4000	>4000	>4000	>4000	>4000	>4000	2.90
6	>4000	>4000	>4000	>4000	>4000	>4000	>4000	>4000	3.60
7	>4000	>4000	>4000	>4000	>4000	>4000	>4000	>4000	1.45
8	>4000	>4000	>4000	>4000	>4000	>4000	>4000	>4000	1.83
9	>4000	>4000	1000 $\pm$ 0.0 [2.5 $\times$ 10 ⁻¹⁰]	2000 $\pm$ 600 [4.9 $\times$ 10 ⁻¹⁰]	2000 $\pm$ 0.0 [4.9 $\times$ 10 ⁻¹⁰]	2000 $\pm$ 0.0 [4.9 $\times$ 10 ⁻¹⁰]	>4000	>4000	2.33
10	>4000	>4000	1000 $\pm$ 0.0 [2.5 $\times$ 10 ⁻¹⁰]	1000 $\pm$ 0.0 [2.5 $\times$ 10 ⁻¹⁰]	2000 $\pm$ 0.0 [4.9 $\times$ 10 ⁻¹⁰]	500 $\pm$ 0.0 [1.2 $\times$ 10 ⁻¹⁰]	260 $\pm$ 0.0 [6.5 $\times$ 10 ⁻¹¹]	130 $\pm$ 0.0 [3.2 $\times$ 10 ⁻¹¹]	2.19
11	>4000	>4000	1000 $\pm$ 0.0 [2.4 $\times$ 10 ⁻¹⁰]	1000 $\pm$ 0.0 [2.4 $\times$ 10 ⁻¹⁰]	2000 $\pm$ 0.0 [4.8 $\times$ 10 ⁻¹⁰]	260 $\pm$ 0.0 [6.3 $\times$ 10 ⁻¹¹]	260 $\pm$ 0.0 [6.3 $\times$ 10 ⁻¹¹]	130 $\pm$ 0.0 [3.1 $\times$ 10 ⁻¹¹]	2.89
Chalcone (fungicide)*	65 $\pm$ 0.0 [3.1 $\times$ 10 ⁻¹¹]	2000 $\pm$ 0.0 [9.6 $\times$ 10 ⁻¹⁰]	1000 $\pm$ 0.0 [4.8 $\times$ 10 ⁻¹⁰]	130 $\pm$ 0.0 [6.2 $\times$ 10 ⁻¹¹]	500 $\pm$ 0.0 [2.4 $\times$ 10 ⁻¹⁰]	260 $\pm$ 0.0 [1.2 $\times$ 10 ⁻¹⁰]	500 $\pm$ 0.0 [2.4 $\times$ 10 ⁻¹⁰]	130 $\pm$ 0.0 [6.2 $\times$ 10 ⁻¹¹]	3.81
IPBC ^b (fungicide)*	2 $\pm$ 0.0 [7 $\times$ 10 ⁻¹²]	2 $\pm$ 0.0 [7 $\times$ 10 ⁻¹²]	2 $\pm$ 0.0 [7 $\times$ 10 ⁻¹¹]	2 $\pm$ 0.0 [7 $\times$ 10 ⁻¹²]	100 $\pm$ 0.0 [3.5 $\times$ 10 ⁻⁸]	2 $\pm$ 0.0 [7 $\times$ 10 ⁻¹²]	1 $\pm$ 0.0 [3.5 $\times$ 10 ⁻¹²]	5 $\pm$ 0.0 [1.7 $\times$ 10 ⁻¹¹]	2.84
	MFC [$\mu\text{g mL}^{-1}$] and [mMol mL^{-1}] ^a								
Compounds	<i>A. niger</i>	<i>A. versicolor</i>	<i>P. variotii</i>	<i>P. funiculosus</i>	<i>T. viride</i>	<i>P. cyclopium</i>	<i>A. pullulans</i>	<i>Ch. globosum</i>	
1	>4000	>4000	>4000	>4000	>4000	>4000	1 $\pm$ 0.0 [2.5 $\times$ 10 ⁻¹²]	>4000	
9	>4000	>4000	1000 $\pm$ 0.0 [2.5 $\times$ 10 ⁻¹⁰]	2000 $\pm$ 600 [4.9 $\times$ 10 ⁻¹⁰]	2000 $\pm$ 0.0 [4.9 $\times$ 10 ⁻¹⁰]	2000 $\pm$ 0.0 [4.9 $\times$ 10 ⁻¹⁰]	>4000	>4000	
10	>4000	>4000	1000 $\pm$ 0.0 [2.5 $\times$ 10 ⁻¹⁰]	1000 $\pm$ 0.0 [2.5 $\times$ 10 ⁻¹⁰]	2000 $\pm$ 0.0 [4.9 $\times$ 10 ⁻¹⁰]	500 $\pm$ 0.0 [1.2 $\times$ 10 ⁻¹⁰]	260 $\pm$ 0.0 [6.5 $\times$ 10 ⁻¹¹]	130 $\pm$ 0.0 [3.2 $\times$ 10 ⁻¹¹]	
11	>4000	>4000	1000 $\pm$ 0.0 [2.4 $\times$ 10 ⁻¹⁰]	1000 $\pm$ 0.0 [2.4 $\times$ 10 ⁻¹⁰]	2000 $\pm$ 0.0 [4.8 $\times$ 10 ⁻¹⁰]	260 $\pm$ 0.0 [6.3 $\times$ 10 ⁻¹¹]	260 $\pm$ 0.0 [6.3 $\times$ 10 ⁻¹¹]	130 $\pm$ 0.0 [3.1 $\times$ 10 ⁻¹¹]	
Chalcone (fungicide)*	65 $\pm$ 0.0 [3.1 $\times$ 10 ⁻¹¹]	2000 $\pm$ 0.0 [9.6 $\times$ 10 ⁻¹⁰]	1000 $\pm$ 0.0 [4.8 $\times$ 10 ⁻¹⁰]	130 $\pm$ 0.0 [6.2 $\times$ 10 ⁻¹¹]	500 $\pm$ 0.0 [2.4 $\times$ 10 ⁻¹⁰]	260 $\pm$ 0.0 [1.2 $\times$ 10 ⁻¹⁰]	500 $\pm$ 0.0 [2.4 $\times$ 10 ⁻¹⁰]	130 $\pm$ 0.0 [6.2 $\times$ 10 ⁻¹¹]	
IPBC ^b (fungicide)*	2 $\pm$ 0.0 [7 $\times$ 10 ⁻¹²]	2 $\pm$ 0.0 [7 $\times$ 10 ⁻¹²]	2 $\pm$ 0.0 [7 $\times$ 10 ⁻¹¹]	2 $\pm$ 0.0 [7 $\times$ 10 ⁻¹²]	100 $\pm$ 0.0 [3.5 $\times$ 10 ⁻⁸]	2 $\pm$ 0.0 [7 $\times$ 10 ⁻¹²]	1 $\pm$ 0.0 [3.5 $\times$ 10 ⁻¹²]	5 $\pm$ 0.0 [1.7 $\times$ 10 ⁻¹¹]	

MIC – minimum inhibitory concentration; MFC – minimum fungicidal concentration. ^a Values are the mean $\pm$ standard deviation of three replicates. ^b *IPBC (3-iodo-2-propynyl butyl carbamate) antimicrobial Preventol® MP100 from Lanxess.

tested compounds showed that in comparison with the starting compounds **2–6**, the new ones **7–11** were shown to be less hydrophobic. As expected, with the extension of the alkyl chain in the C-10 position, the lipophilicity of the molecules increases. Compounds **2–6** have lipophilicity at the range of 2.17–3.60. To be able to make some comparison between the tested derivatives with the shortest (**2** and **7**) and the longest alkylthio chains (**6** and **11**), their molecules (the molecular surface for space-filling CPK models) are visualized in Fig. S11 and S12.† Because the most potent derivatives were determined to be **9–11**, both as cytotoxic and fungicidal agents, we suggested that the amino NH₂ substituent at C7, the longer alkylthio chain at C10 and the lipophilicity in the range of 2.19–2.89 are optimal for their biological activity.

Molecular docking was performed to study the molecular mechanism of binding for the synthesized series of compounds. Compound **11**, which globally showed the best anticancer and antifungal profile, was selected to visualize the key molecular interactions within protein targets responsible

for anticancer and antifungal activity. The colchicine- β -tubulin complex (PDB ID: 1SA0) was used to assess the potential of compounds **2–11** as anticancer agents and as templates for homology modeling of the β -tubulin of the tested fungus. Docking studies revealed that the binding modes of the compounds with the highest anticancer activity are coherent with the co-crystallized colchicine (Fig. 2A). The trimethoxyphenyl ring of **11** lies in the β -subunit occupying the same position as the corresponding ring of colchicine. To evaluate the antifungal activity, the homology models of β -tubulin for all the fungi were generated and used in the molecular docking study. It should be noted that adding an alkylthio chain at C10 led to rotation of the colchicine ring in the binding site exposing the alkylthio substituent to the hydrophobic cavity formed by Lys254 β , Val181 α and Thr179 α residues. Six out of the eight tested strains showed more than 80% similarity to human β -tubulin (Table S1†), whereas, one (*A. pullulans*) showed only approx. 41% similarity. In general, the binding mode of **11** in species, where it showed the highest antifungal activity (*i.e.* *P. cyclopius*, *A. pullulans*, and

Fig. 2 The comparison of the binding mode of **11** (magenta) with colchicine (green) in the human β -tubulin binding site (A) and with chalcone (yellow) in the *Ch. globosum* β -tubulin binding site (B).

Ch. globosum) was coherent, however, different than in human β -tubulin (Fig. 2B).

The closest inspection of the binding sites indicated that several mutations occurred between human and fungal tubulins. The common mutations are Ala316Ser, Val318Ile and Asn167Ala, whereas two specific mutations (Cys241Ser and Ile378Val) occurred only in species where **11** showed the highest activity.

The exchange of cysteine 241 to serine leads to the formation of a stronger hydrogen bond with the methoxyl group of compound **11**, while mutation to alanine 167 causes, mainly, deepening of the binding pocket (the comparison of binding pocket shapes is presented in Fig. S14†).

Conclusions

In conclusion, we showed that a simple two-step reaction leads to new deacetyl alkylthiocolchicine derivatives with biological properties. Deacetylation of colchicine derivatives increased their biological activity, both in terms of cytotoxic and fungicidal properties. 7-Deacetyl-10-*i*-propylthiocolchine and 7-deacetyl-10-*n*-butylthiocolchicine show cytotoxic activity against the SKOV-3 ovarian cell line compared to the known 7-deacetyl-10-methylthiocolchinine. Moreover, in contrast to 10-alkylthiocolchicines which were completely inactive against all the tested fungi species, all the new deacetyl derivatives were shown to be active against *A. pullulans* and *Ch. globosum*. Additionally, the derivatives with longer alkyl chains, 7-deacetyl-10-*n*-propylthiocolchicine and 7-deacetyl-10-*n*-butylthiocolchicine, were active against four additional fungi strains. Among the compounds with a propylthio substituent, the one with an unbranched alkylthio chain was more active than the one with an *i*-propylthio substituent. All these findings have suggested that further modifications of

this group of colchicine derivatives could lead to more active compounds with greater potential as drug candidates.

Conflicts of interest

There are no conflicts to declare.

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