Design, synthesis, spectral and theoretical study of new bile acid–sterol conjugates linked via 1,2,3-triazole ring

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ABSTRACT

New four steroid conjugates have been prepared from bile acids and sterol derivatives using click chemistry method. The azide-alkyne Huisgen cycloaddition (intermolecular 1,3-dipolar cycloaddition) of the propargyl ester of lithocholic, deoxycholic, cholic acid as well as dehydrocholic acids and azide derivatives of cholesterol gave a new bile acid–sterol conjugates linked with a 1,2,3-triazole ring. Previously, bile acids were converted into bromoacetyl substituted derivatives by the reaction of propargyl esters of lithocholic, deoxycholic, cholic with bromoaectic acid bromide in toluene with TEBA and sodium hydride. All conjugates were obtained in good yields using an efficient synthesis method. The structures of all products were confirmed by spectral (1H- and 13C NMR, and FT-IR) analysis, mass spectrometry (ESI-MS), as well as PM5 semiempirical methods. Estimation of the pharmacotherapeutic potential has been accomplished for the synthesized compounds on the basis of Prediction of Activity Spectra for Substances (PASS).

1. Introduction

Among the vast number of compounds of natural origin one of the most important groups are steroids. This group are a large class of very important compounds which display very significant roles in different organisms. The most famous steroid is cholesterol. It is constituent of the cell membrane and it’s present in large concentrations in the brain and nervous tissue [1–4]. This sterol is the biosynthetic precursor of vitamin D, bile acids, steroid hormones and lipoproteins [5–7]. All sterols are crystalline with a secondary hydroxyl group in the position C(3) of the steroid skeleton. This group located in the plane of the A/B rings forms β-sterols. Ring A/B of the steroid skeleton may form an allo (trans geometry) or normal series (cis geometry). Moreover this class of compounds has differently modified side chains and one or two double bonds [8–10]. In turn, bile acids have preferred hydroxyl groups on the C(3) position in the α orientation. These compounds and their derivatives have a large, inflexible, and curved skeleton. Additionally, bile acids have chemically different polar hydroxyl groups 3α or 3α,7α and 3α,12α as well as 3α,7α,12α which are responsible to some extent for their amphiphilic properties. This specific structure makes that bile acids are common in the study of biomimetic chemistry, host–guest chemistry or molecular recognition as well as in supramolecular chemistry and as drugs in pharmacology [11,12]. Bile acids themselves have been used as building blocks for the design and construction of new molecular receptors that are able to recognize guest molecules of various chemical character. Simultaneously bile acid dimers can be used for the synthesis of different macrocyclic molecules as artificial receptors [13–17]. On the other hand some derivatives of bile acids are very good organogelators [11,18–20].

Due to the specific and amazing properties of bile acids and the triazole ring, various conjugates containing amino acid [21,22], nucleosides [23–25] sugar [26], as well as β-lactam [27] in the structure were synthesized. Whereas the connection of molecules of bile acids with cholesterol by the 1,2,3-triazole ring allows the synthesis of novel conjugates with a multitude of applications [28]. Synthesis of new steroid conjugates entails the possibility of receiving more compounds with high biological activity [29].

The „click” chemistry is very beautiful part of modern organic synthesis. It includes a general field of carbon–heteroatom bond forming reactions that fulfill specified requirements such as very simple reaction conditions, high efficiency and selectivity as well as simple product isolation [30]. Another extremely important argument in favor of such a synthesis is fact, that products are stable in various solvents, including water [30,31]. One of the more important methods of preparing a 1,2,3-
triazole ring is Huisgen 1,3-dipolar cycloaddition. The reaction occurs
between azides and terminal alkynes and it is the copper(I) catalyzed
[32,33].

Compounds of this type are very resistant to the hydrolysis, oxidation
and reduction conditions of metabolic degradation. The Cu(I)-catalyzed
“click” reaction is thus an extremely useful method to obtain new 1,2,3-
triazole derivatives of bile acids [34–39]. These five-membered het-
erocyclic rings can form intra- or intermolecular hydrogen bonds
together with dipole–dipole interactions with an increase in the solu-
bility of conjugates and facilitate binding of molecular targets [40].

2. Experimental

2.1. Instrumentation and chemicals

All of the synthesis reagents lithocholic, deoxycholic, cholic and
dehydrocholic acids, cholesterol, propargyl alcohol, bromoacetic acid
bromide, N,N’-Dicyclohexylcarbodiimide, 4-dimethylaminopyridine,
sodium azide, sodium hydroxide, benzyltriethylammonium chloride,
sodium ascorbate were purchased from Sigma-Aldrich Corporation.
Solvents chloroform, dichloromethane, toluene, hexane, t-butanol,
methanol were obtained from common com-mercial sources (Merck,
Fisher) and used without purification. General IR Spectra: FT/IR
[32,33].

2.2. Synthesis

Molar ratios of the respective reactants are shown in Table 1.

Procedure for propargyl esters of bile acids: the bile acids (lithocholic
1, deoxycholic 2, cholic 3, dehydrocholic 4) was dissolved in 15 mL of
dichloromethane. Then, propargyl alcohol, DCC and DMAP was added
and the reaction was carried out for 24 h at room temperature. Next the
mixture washed with cool water, extracted ethyl acetate and washed
and the reaction mixture was kept at room temperature for 24 h. Then the excess of sodium hydroxide was filtered (then neutralize
it with anhydrous methanol), and the filtrate was washed with NaHCO
(5%, 20 mL), brine (200 mL) and finally dried over Na
2

Procedure for dimers of bile acids and cholesterol derivatives
(15–18): compounds (8–11) was dissolved in a mixture of t-BuOH/MeOH
(6 mL, 5:1). Then, cholesterol-3β-yl 2-bromoacetate (13) was added.
Next, to the homogenous mixture were added CuSO
4
H2O (3 mg, 3 mol %)
and sodium ascorbate (9 mg, 20 mol%) in water (0.3 mL). The re-
action mixture was heated at 60 °C for 8 h and then extracted with chloroform, washed with brine and dried over anhydrous Na
2
SO
4
The crude compound was purified by column chromatography on silica gel
using chloroform/ethyl acetate (5:1) as an eluent.

2.3. Chemical characterisation

2.3.1. Propargyl dehydrocholate (8)

Yield: 92%, crude. Melting point: 183–184 °C. Molecular mass (g/
mol), calculated for C
2
H
2
O
2
: 440.26. ESI–MS (MeOH): m/z 496 [M +
C
1
H
1
O
1
H
1
] +, 463 [M + Na] +. IR (solid state) ν, cm
-1
: 3305, 2928, 2863, 1724, 1247. H NMR (400 MHz, CDCl
3
): δ 4.68 (dd, J = 2.5, J2 = 0.8 Hz, 2H, CH
2–25
), 2.47 (t, J = 2.5 Hz, 1H, C
=CH
), 1.40 (s, 3H, CH
2–19
), 1.07 (s, 3H, CH–18), 0.85 (d, J = 6.5 Hz, 3H, CH–21). 13C
NMR (75 MHz, CDCl
3
): δ 211.91, 209.08, 208.71, 173.17, 77.77, 74.73,
56.86, 51.78, 51.71, 48.96, 46.83, 45.58, 45.50, 44.97, 42.78, 38.62,
36.48, 35.99, 35.43, 35.25, 31.20, 30.26, 27.61, 25.11, 21.90, 18.60,
11.83.

2.3.2. Propargyl 3α,12α-dibromoacetoxacyclopent-5-yl-cholane-24-oate (10)

Yield: 54%, crude. Oil. Molecular mass (g/mol), calculated for
C
3
H
14
Br
4
O
2
: 762.15. ESI–MS (MeOH): m/z 711 [M + K]+, 695 [M +
Na]+. IR (oil) ν, cm
-1
: 3292, 2931, 2866, 1727, 1276. H NMR (400
MHz, CDCl
3
): δ 5.16 (t, J = 2.6 Hz, 1H, 12β–H), 4.81–4.80 (m, 1H, 3β–H),
4.67 (dd, J1 = 2.5, J2 = 0.8 Hz, 2H, OCH
2
), 3.89 (s, 2H, 12α–CH
2
Br),
3.80 (s, 2H, 3α–CH
2
Br), 2.48 (t, J = 2.5 Hz, 1H, C=CH
), 0.92 (3H, 3,8

Table 1

| Reagents | mmol of reagents | Product | Ref. |
|-----------------|------------------|---------|------|
| Reagents | mmol | 1 | 2 | 3 | 4 | | |
| (1) | HC≡CCH
2
OH | DCC | DMAP | 1.3 | 2.1 | 13.6 | 0.3 | (8) | [41,42] |
| (2) | 1.3 | 2.1 | 13.6 | 0.3 | (6) | [23] |
| (3) | 1.3 | 2.1 | 13.6 | 0.3 | (7) | [23] |
| (4) | 1.3 | 2.1 | 13.6 | 0.3 | (8) | – |
| (5) | BrCH
2
COBr | NaH | TEB4 | 0.6 | 0.7 | 1.8–3.0 | 0.1 | (9) | [37] |
| (6) | 0.6 | 1.3 | 1.7–2.9 | 0.06 | (10) | – |
| (7) | 0.6 | 1.9 | 1.7–2.8 | 0.06 | (11) | – |
| (12) | 0.6 | 0.7 | 1.9–3.2 | 0.07 | (13) | [43] |
| (13) | NaN | – | – | 0.5 | 2.9 | – | – | (14) | [44] |
| (8) | 0.5 | 0.5 | – | – | (15) | – |
| (9) | – | – | 0.5 | – | (16) | – |
| (10) | 0.3 | 0.5 | – | – | (17) | – |
| (11) | 0.2 | 0.5 | – | – | (18) | – |
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2.3.4. 2-[(2-(cholest-5-en-3-yloxy)-2-oxoethyl)-1H-1,2,3-triazol-4-yl] C

31.51, 30.81, 30.51, 29.69, 28.44, 27.17, 26.30, 26.21, 25.97, 24.88, 17.45, 11.96, 11.82.

2.4. 3.1. Synthesis

2.3.7. 1-[(2-cholest-5-en-3-yl)-2-oxoethyl]-1H-1,2,3-triazol-4-yl] methyl 3,7-dioxo-hydroxycholan-24-acetate (18)

Yield: 78%. Oil. Molecular mass (g/mol), calculated for C_{49}H_{42}BrN_{12}O_{7}: 1090.62 g/mol. IR (oil) (cm^{-1}): 1741, 1731, 1707, 1675, 1646, 1638, 1625, 1606, 1577, 1564, 1550, 1537, 1522, 1438, 1383, 1372, 1350, 1282, 1157, 1133, 1112, 1071, 1053, 1022, 926, 894, 867, 831. C NMR (75 MHz, CCl_{4}): 328.16, 292.15, 277.24, 172.74, 131.78, 97.90, 52.68, 49.94, 48.03, 45.21, 42.49, 40.28, 37.54, 36.63, 35.74, 35.44, 34.72, 21.84, 19.82, 17.44, 11.78, 11.72.
3.2. Spectroscopic study

3.2.1. Nuclear magnetic resonance spectroscopy

The two substrates—propargyl 3α-bromoaacetoxyl-5β-cholan-24-oate (9) and cholesteryl-3β-yl-2-azidoacetate (14)—have been described and characterized in the literature [37,44].

The $^1$H and $^{13}$C NMR data of compounds (8), (10), (11) and (15–18) are shown in Tables 2 and 3, respectively. The $^1$H NMR spectra in the region of 5.45–4.60 ppm for the most characteristic signals of compounds (15–18) are shown in Fig. 1.

In the $^1$H NMR spectrum of dehydrocholic propargyl ester (8) showed characteristic two hydrogen singlets in the range 1.07 and 1.40 ppm and doublet at 0.85 ppm assigned to CH$_3$–18, CH$_3$–19, and CH$_2$–21, respectively. The protons of the CO$_2$CH$_2$ group gave signals in the range 4.68 ppm. Whereas the terminal proton in propargyl group gave characteristic signal at 2.47 ppm. The $^1$H NMR spectra of compounds (10) and (11) show characteristic multiplets in the range 4.81–4.63 ppm assigned to axial positions of the C3β–H protons in steroid skeleton. In the spectrum of compound (11) additionally is present doublet of the C7β–H proton at 5.01 ppm. However, in the case of these bromoacetates derivatives protons of C12β–H appear as triplets in the range of 5.17–5.16 ppm. The $^1$H NMR spectra of these compounds show characteristic singlets in the range 3.80–3.79 ppm for the protons of the 3α–CO$_2$CH$_2$Br group, whereas for compound (11) characteristic doublets at 3.85 ppm for the protons of the 7α–CO$_2$CH$_2$Br group are observed. However, protons of 12α–CO$_2$CH$_2$Br group for both compounds appear as a singlet at 3.89 ppm. The doublet of doublets of CO$_2$CH$_2$ protons at 4.67 ppm for both discussed derivatives were observed in $^1$H NMR spectra. The protons of C=C–CH$_3$ group gave signals in the range 2.48–2.47 ppm. Two hydrogen singlets in the range of 0.76–0.75 and 0.94–0.92, as well as characteristic doublets at 0.85–0.83 ppm are assigned to CH$_3$–18, CH$_3$–19, and CH$_2$–21, respectively.

The diagnostics proton signals of the triazole ring C27–H of all conjugates with 1,2,3-triazole ring (15–18) in CDC$_3$ arise as a singlet at about 7.76–7.75 ppm. In turns, the protons of the methylene groups C25–H as well as C28–H linked directly to the triazole ring give signals in the range 5.24 ppm and 5.14 ppm, respectively. The $^1$H NMR spectra of (15–18) showed characteristic multiplets of protons of C3’α–H of sterol skeleton in the range of 4.89–4.59 ppm. In the same range there are also multiplets from the protons of C3β–H group of bile acid skeleton.

In the spectra of compounds (16) and (17) characteristic broad singlets in the range 5.14 ppm are observed which are due to the C12β–H protons. $^1$H NMR spectra of conjugate (17) show singlet at 5.01 ppm assigned to the C7β–H protons of the bile acid skeleton.

In the bile acids skeleton was observed two hydrogen singlets ranking from 1.05 to 0.62 and 1.40–0.90 ppm and characteristic doublet at 0.85–0.79 ppm assigned to CH$_3$–18, CH$_3$–19 and CH$_2$–21, respectively. On the other hand in the cholesterol part the characteristic hydrogen singlets at 0.68 assigned to CH$_3$–18. The second sets of singlets at 1.02 ppm were assigned to CH$_3$–19. The characteristic doublet of CH$_2$–21’ are at 0.93–0.91 in the all conjugates. The $^1$H NMR spectra of (15–18) showed a doublet at 0.86 ppm for the protons of the CH$_3$–26’.
and CH₂–27° methyl groups. For cholesterol derivatives, it is diagnostically detectable for C6′–H at 5.39–5.38 ppm. Additionally, the ¹H NMR spectra of compounds (15–18) show diagnostic singlets in the range 3.80–3.79 ppm for the protons of the 3α–CO₂CH₂Br group, whereas for compound (17) a characteristic signal at 3.85 ppm for the protons of the 7α–CO₂CH₂Br group is observed. However, in the case of bromoacetoxy groups in positions 3α, 7α, CH₂–Br groups are observed. However, protons of 12α–CO₂CH₂Br and 26α–CO₂CH₂Br groups were situated in the ranges of 56.05–56.02 ppm and 49.89–49.13 ppm, respectively. The characteristic protons shifts for compounds (15–18) are collected in Table 2.

On the other hand, carbon atoms of bromoacetoxy groups in positions 3α or 12α resonate in the range of 166.75–166.28 ppm. Unusually, a relationship was observed between the signals of carbon atoms C(3) and C(12) of the steroid skeleton. The carbon atoms of the C(12) steroid skeleton gave signals in the range of 76.60–76.60 and the C(3) 75.85–7.73 ppm. However, carbon of the C(7) gave signal at 73.06 ppm. The diagnostic signal for BrCH₂ groups is observed at 27.29–25.97 ppm.

The ¹³C NMR spectra of dimers linked by 1,2,3-triazole ring in CDCl₃ showed signals at 12.25–11.80 ppm, 23.78–21.85 ppm, 18.57–17.40 ppm, which were assigned to CH₃–18, CH₃–19 and CH₃–21 of bile acids parts, respectively. In the case of cholesterol parts, the signals of C-atoms of CH₂–18′, CH₂–19′ and CH₂–21′ groups were situated in the ranges of 11.82–11.77, 19.24–19.22, and 18.67–18.65 ppm, respectively. The following characteristic shifts of methyl groups were present in the steroid side chain: CH₃–26 and CH₃–27 are positioned in the range of 22.80–22.78 ppm and 23.77–22.51 ppm. Analytical differences in the ¹³C NMR spectra of the methyl groups of compound (15) are shown in Fig. 2. On the other hand, in the ¹³C NMR spectra of compounds (15–18), the signals of the C(25)H₂ and C(28)H₂ groups appeared in the range of 56.05–56.02 ppm and 49.89–49.13 ppm, respectively. The carbon atoms from triazole ring: C(26) as well as C(27) groups resonated at 143.34–143.16 ppm and 125.16–125.11 ppm, respectively. The signals of C(24) = O and C(29)=O, appeared in the range of 174.10–173.79 ppm and 165.49–165.45 ppm, respectively. However, carbon atoms of bromoacetoxy groups in positions 3α, 7α or 12α resonate in the range of 166.75–166.26 ppm. The signals for carbons in BrCH₂ groups are observed at 28.41–27.97 ppm.

3.2.2. Infrared spectroscopy

The most characteristic feature of the FT-IR spectra of compounds (8), (10) and (11) are bands at 3305 cm⁻¹ as well as 3292 and 3286 cm⁻¹ assigned to the υ(≡C–H) group. The steroid skeleton itself, being a saturated hydrocarbon, is not a source of many useful IR features. Any vibrational bands due to C–C bonds were very weak and were lost among others in the fingerprint region. Stretching vibrations of C–H bonds merged into one broad band, for conjugate structure, between 2931 and 2863 cm⁻¹. For these three substrates are important and analytical bands at 1727–1724 cm⁻¹, which are due to the symmetric carbonyl group υ(C=O) stretching vibration appears in the FT-IR spectrum. Moreover strong characteristic bands in the region 1279–1247 cm⁻¹ are present, which are assigned to the υ(C=O).

Fig. 3. Molecular models of conjugates (15–18) calculated using the PMS method.
It should be noted, that the most characteristic in the FT-IR spectra of (15–18) are two strong bands in the 1746–1719 cm\(^{-1}\) and 1277–1272 cm\(^{-1}\) region are present, which are assigned to the \(\nu(C=O)\) and \(\nu(C\cdots O)\), respectively. In turn, the C–C strong bands were rather weak for all conjugated steroids, and they were observed at 1650, 1653, 1664 and 1662 cm\(^{-1}\), respectively.

In all spectra of conjugates there are also visible bands related to vibrations of C–H bonds in the region 2935–2863 cm\(^{-1}\).

3.3. PM5 calculations

PM5 semiempirical calculations were performed using the

![Molecular models of selected conjugates (15) and (18) calculated by PM5 method four molecules.](image-url)
WinMopac 2003 program. The final heats of formation (HOF) for compounds (15–18) are presented in the Table 4. The molecular models of all conjugates are shown in Fig. 3. In many works that describe the application of computational methods, one can find information on the comparison of theoretical results with crystallographic structures. Not without significance is the use of computational methods in determining the properties of the docking [48–50]. We were able to obtain a very good picture of molecular modeling using semiempirical calculations [51]. The lowest HOF values were observed for cholic acid derivatives (17), where the OH groups facilitate the formation of intramolecular H-bonds and stable host–guest complexes. These complexes may be stabilized by H-bonding or electrostatic interactions that arise from the OH groups in the bile acid molecule. The HOF value decreases with the increasing number of OH groups in the steroid skeleton. It should be noted that in the case of the dehydrocholic acid derivative, the heat of formation is similar to that of the deoxycholic acid derivative. The lower HOF value for derivative (18) can be explained by the greater stability of the carbonyl group, which is also noticed for free acids (2) and (4), respectively. Derivative (18) cannot be hydrogen atoms donor in the formation of hydrogen bonds, therefore such HOF values were observed.

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**Scheme 1.** Synthesis of propargyl esters (5–8) of bile acids (1–4), bromoacetyl substituted derivatives of propargyl esters of bile acids (9–11) and bromoacetyl substituted derivative of cholesterol (13) as well as its azidoacetyl substituted derivative (14).

**Scheme 2.** Synthesis of dimers of bile acids and cholesterol derivatives (15–18) linked by 1,2,3-triazole ring.

**Table 2**

| No. of atoms | 8  | 10  | 11  | 10  | 11  | 18  | 21  | 24  | 25  | 26  | 27  |
|--------------|----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
|              | $^1$H | $^{13}$C | $^1$H | $^{13}$C | $^1$H | $^{13}$C | $^1$H | $^{13}$C | $^1$H | $^{13}$C | $^1$H | $^{13}$C |
| 3            | 208.71 | 4.81–4.80 | 75.73 | 4.70–4.63 | 75.85 | 4.70–4.63 | 75.85 | 4.70–4.63 | 75.85 | 4.70–4.63 | 75.85 | 4.70–4.63 |
| 7            | 209.08 | –                  | –                          | 5.01 | 73.06 | 5.01 | 73.06 | 5.01 | 73.06 | 5.01 | 73.06 | 5.01 |
| 12           | 211.91 | 5.16                  | 76.22                          | 5.17 | 76.60 | 5.17 | 76.60 | 5.17 | 76.60 | 5.17 | 76.60 | 5.17 |
| 3α-CH$_2$Br  | –                  | 3.80                          | 27.29                          | 3.79 | 26.30 | 3.79 | 26.30 | 3.79 | 26.30 | 3.79 | 26.30 | 3.79 |
| 7α-CH$_2$Br  | –                  | –                          | –                          | 3.85 | 26.21 | 3.85 | 26.21 | 3.85 | 26.21 | 3.85 | 26.21 | 3.85 |
| 12α-CH$_2$Br | –                  | –                          | –                          | 3.89 | 26.70 | 3.89 | 26.70 | 3.89 | 26.70 | 3.89 | 26.70 | 3.89 |
| 3α-CO        | –                  | –                          | –                          | 166.67 | 166.75 | 166.67 | 166.75 | 166.67 | 166.75 | 166.67 | 166.75 |
| 7α-CO        | –                  | –                          | –                          | 166.53 | 166.57* | 166.53 | 166.57* | 166.53 | 166.57* | 166.53 | 166.57* |
| 12α-CO       | –                  | –                          | –                          | 166.53 | 166.57* | 166.53 | 166.57* | 166.53 | 166.57* | 166.53 | 166.57* |
| 18           | 1.07 | 11.83 | 0.75 | 12.74 | 0.76 | 12.01 | 0.76 | 12.01 | 0.76 | 12.01 | 0.76 | 12.01 |
| 19           | 1.40 | 21.90 | 0.92 | 22.82 | 0.94 | 22.21 | 0.94 | 22.21 | 0.94 | 22.21 | 0.94 | 22.21 |
| 21           | 0.85 | 18.60 | 0.83 | 17.35 | 0.85 | 17.47 | 0.85 | 17.47 | 0.85 | 17.47 | 0.85 | 17.47 |
| 24           | –    | 173.17 | –    | 173.16 | –    | 173.12 | –    | 173.12 | –    | 173.12 | –    | 173.12 |
| 25           | 4.68 | 51.71 | 4.67 | 51.74 | 4.67 | 51.83 | 4.67 | 51.83 | 4.67 | 51.83 | 4.67 | 51.83 |
| 26           | –    | 77.77 | –    | 77.85 | –    | 77.71 | –    | 77.71 | –    | 77.71 | –    | 77.71 |
| 27           | 2.47 | 74.73 | 2.48 | 74.72 | 2.47 | 74.80 | 2.47 | 74.80 | 2.47 | 74.80 | 2.47 | 74.80 |
were predicted for a potential compound with the highest probability. Biological activity spectra were predicted for all four synthesized compounds. Cholesterol antagonist, antineoplastic and glyceryl-ether monooxygenase inhibitor; 4 – antieczematic activity, 5 – antihypoproteinemic; 6 – hypolipemic; 7 – biliary tract disorders treatment; 8 – antiinfertility female; 9 – UGT1A4 substrate.

3.4. Prediction of activity spectra for substances

Potential pharmacological activities of the synthesized conjugates have been determined on the basis of a computer-aided drug discovery approach with in silico Prediction of Activity Spectra for Substances (PASSs) program [52–55]. In previous works were presented and discussed in silico studies of steroid conjugates with different long chain amines, as well as linked triazole rings [39,44,56–59]. In this work, the biological activity spectra were predicted for all four synthesized conjugates (15–18) with PASS. Furthermore, the types of activity, which were predicted for a potential compound with the highest probability (focal activities), have also been selected. They are presented in Fig. 5. According to these data, the most frequently predicted types of biological activity are the cholesterol antagonist, antineoplastic and glyceryl-ether monoxygenase inhibitor beyond conjugate (18). On the other hand conjugate (15) is only antieczematic activity, (18) dermatologic, antiinfertility female, UGT1A4 substrate and (17) only to hypolipemic and biliary tract disorders treatment, respectively.

4. Conclusions

In summary, four new conjugates of bile acids and cholesterol linked with 1,2,3-triazole ring (15–18) were prepared from propargyl esters of bile acids and azidoacetyl substituted derivative of cholesterol in t-butanol/methanol mixture in the presence of sodium ascorbate and CuSO₄•H₂O at 60 ◦C. Additionally propargyl dehydrocholate (8) as well as two bromoacetil substituted derivatives of bile acids (10) and (11) were prepared from dehydrocholic acid and propargyl alcohol in DCC, DMAP in dichloromethane and propargyl esters of lithocholic, deoxycholic as well as cholic acid and sodium hydride, TEBA in tolugene with bromoacetic acid bromide, respectively. These compounds were characterized by spectroscopic (NMR, FT-IR) and molecular structure (PMS) methods. These new conjugates modified by a triazole ring can be used in the molecular recognition, supramolecular chemistry, and in pharmacology [26,29,60–62]. In addition, they could find applications as artificial receptors [61,62], good organogelators [29], as well as novel drugs [30].
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