Synthesis of Pharmacological Heterocyclic Derivatives Based Surfactants

Refat El-Sayed1,2* and Ahmed. A Fadda3

1 Department of Chemistry, College of Applied Sciences, Umm Al-Qura University, 21955 Makkah, SAUDI ARABIA
2 Department of Chemistry, College of Science, University of Benha, EGYPT
3 Department of Chemistry, Faculty of Science, Mansoura University, Mansoura, 35516, EGYPT

Abstract: Synthesis of chromenopyrimidine derivatives and the related fused system carried out by the reaction of chromene derivative 1 with various reagents under suitable reaction conditions. Condensation of stearoyl chloride with these heterocycles, then, propoxylated the products using propylene oxide to produce surface active agents having a twofold capacity as surface and antimicrobial dynamic specialists which may be served in the production of medications, pesticides, beautifying agents or may be utilized as an antimicrobial. Some of the surface properties and antimicrobial activity were resolved.

Key words: synthesis, heterocycles, antimicrobial and surface activities

1 INTRODUCTION

Many of pharmacologically active heterocyclic compounds are necessary for the synthesis of bioactive molecules1-2. Chromene derivatives represent a favorite structural motif well-distributed in natural products with a broad spectrum of potent biological activities3. Chromene derivatives are using in the synthesis of a variety of heterocyclic compounds that uses as a raw material for the drug synthesis4-6. Fused chromenes are very important constituents that exhibited a broad spectrum of biological activities such as antimicrobial7,8, antiviral9, antitumor10, and inhibitors of influenza virus sialidases11. Aminochromenes are being the main components of very natural products and they have established increasing attention in recent years due to their antimicrobial activities of the interest family of heterogeneous exhibitions as anticancer, antioxidant activities and promising therapeutic drugs among other applications12,13.

Oleochemicals are essential to different industries such as coatings, surfactants, plasticizers, lubricant additives, pharmaceuticals, soaps, detergents, textiles, plastics, organic pesticides and cosmetic formulations14-21. In continuation, as extended of our research program towards the development of highly expedient, efficient methods to syntheses of diverse heterocyclic compounds22-29. The interesting properties of chromene and fatty acids led us to investigate an efficient synthesis with the goal of obtaining more potent surface and pharmacologically active compounds.

2 EXPERIMENTAL

Each melting point is in degrees Celsius and have been identified on the electric Gallenkamp melting point apparatus. IR spectra were recorded on the Pye Unicam SP-1000 cm−1 using KBR chip technology. 1H NMR spectra were measured in Bruker WP 300 MHz (CDCl3) and / or Bruker AC 300 spectrometer (Fällanden, Switzerland) that operate in the 400 MHz (DMSO-d6) as a solvent using TMS as internal reference. Mass spectra were determined on GC-MS. QP-100 EX Schimadzue (Japan) in the unity of analytical minute, Faculty of Science, Cairo University, Egypt. Conducted microscopic analysis component of the use of CHNS tools model elemental analyzer EA3000 EURO VECTORS and biological activity was detected in College of Applied Sciences, Umm Al Qura University, Saudi Arabia.

2.1 Synthesis

2.1.1 Synthesis of 2-(4-amino-8-hydroxy-5-(4-hydroxyphenyl)-5H-chromeno[2,3-d]pyrimidin-2-yl)acetonitrile (2).

A solution of chromene 1 (2.8 g, 10 mmol) in absolute ethanol (25 mL) and malononitrile (0.66 g, 10 mmol) was heated under reflux for 6 h in the presence of pipedine (2 drops). The mixture left overnight, then, filtered, dried...
and recrystallized from ethanol. Brawn crystals yield (80%), m.p. 183-185°C. IR (v/cm⁻¹): broad bands at 3475, 3426 (OH), 3405, 3389 (NH2) and 2206 (CN); 1H NMR (DMSO-d6): δ: 9.29 (s, 2H, CH2), 4.68 (s, 1H, CH-4 pyran), 6.48 (s, 2H, NH), 7.20-8.40 (m, 7H, ArH), 9.20 (s, 1H, OH), 9.90 (s, 1H, OH). MS (m/z, %): (347, 24.92). Anal. Calcd. (%) for C9H13N2O2: C, 72.10; H, 6.02; N, 13.20. Found: C, 72.15; H, 5.89; N, 12.90.

2.1.2 Synthesis of 4-amino-5-(4-hydroxyphenyl)-5H-chromeno[2,3-d]pyrimidine-8(1H)-one (3)

A mounts of chromene 1 (2.8 g, 10 mmol) and formamide (20 mL) heated under reflux at 110°C for 24 h. After cooling, the mixture diluted with water (50 mL) and neutralized with dil. HCl, then, filtered recrystallized from ethanol. Red solid; yield (70%), mp 210-213°C. IR (v/cm⁻¹): 3434, 3402 (OH), 3372, 3396 (NH2), 1610 (C = N). 1H NMR (DMSO-d6): δ: 4.98 (s, 1H, OH pyran), 7.20-8.20 (m, 9H, ArH and NH), 9.10 (s, 1H, OH), 9.92 (s, 1H, OH). MS (m/z, %): (308, 50.98). Anal. Calcd. (%) for C9H13NO2: C, 72.10; H, 6.02; N, 13.20. Found: C, 72.15; H, 5.89; N, 12.90.

2.1.3 Synthesis of 8-hydroxy-5-(4-hydroxyphenyl)-3H-chromeno[2,3-d]pyrimidine-4(5H)-one (4)

An excess of formic acid (20 mL) and chromene 1 (2.8 g, 10 mmol) heated on sand bath at 120°C for 12 h. After complete the reaction (monitored by TLC), evaporated the solvent under pressure, then, the obtained solid purified from ethanol. Red solid; yield (20%), mp 150-152°C. IR (v/cm⁻¹): 3434, 3372 (OH), 3200 (NH stretching), 1654 (C = O), 1607 (C = N); 1H NMR (DMSO-d6): δ: 4.71 (s, 1H, CH-4 pyran), 7.20-8.40 (m, 7H, ArH), 8.80 (s, 1H, CH of pyrimidine), 9.20 (s, 1H, OH), 9.90 (s, 1H, OH), 11.38 (s, 1H, NH). MS (m/z, %): (308, 80.95). Anal. Calcd. (%) for C9H13NO2: C, 72.10; H, 6.02; N, 13.20. Found: C, 72.15; H, 5.89; N, 12.90.

2.1.4 Synthesis of 8-hydroxy-5-(4-hydroxyphenyl)-4-imino-3-phenyl-3,4-dihydro-1H-chromeno[2,3-d]pyrimidine-2(5H)-thione (5)

Equimolar amounts of chromene 1 (1.4 g, 5 mmol) and phenyl isothiocyanate (0.6 mL) in dry ethanol (15 mL) containing of triethylamine (2 drops) heated under reflux for 11 h. The formed solid collected after evaporation of the solvent, then, recrystallized from ethanol. Yellow solid; yield (75%), mp 125-130°C. IR (v/cm⁻¹): broad 3480, 3415 (OH), 3353, 3216 (two NH), 1332 (C = S). 1H NMR (DMSO-d6): δ: 4.69 (s, 1H, CH-4 pyran), 7.20-8.40 (m, 7H, ArH), 9.00 (s, 1H, OH), 9.40 (s, 1H, imino NH), 9.79 (s, 1H, OH), 11.18 (s, 1H, NH). MS (m/z, %): (415, 50.34). Anal. Calcd. (%) for C17H13N3O4S: C, 48.86; H, 3.34; N, 12.80; S, 24.00. Found: C, 48.86; H, 3.34; N, 12.80; S, 24.00.

2.1.5 Synthesis of 8-hydroxy-5-(4-hydroxyphenyl)-4H-chromeno[2,3-d]pyrimidine-2,4(3H,5H)-dithione (6)

A mixture of chromene 1 (2.8 g, 10 mmol) and carbon disulphide (10 mL) in dry ethanol (10 mL) containing KOH (1 g) heated under reflux for 2 h. After evaporation the excess of solvent, the obtained solid washed with water/HCl, then, filtered, dried and recrystallized from ethanol. Dark brown solid; yield (35%), mp 243-245°C. IR (v/cm⁻¹): two broad bands at 3475, 3324 (OH), 2222, 3188 (NH); 1H NMR (DMSO-d6): δ: 5.12 (s, 1H, CH-4 pyran), 7.20-8.40 (m, 7H, ArH), 9.15 (s, 1H, OH), 9.80 (s, 1H, OH), 10.60 (s, 1H, NH), 11.20 (s, 1H, OH). MS (m/z, %): (356, 68.89). Anal. Calcd. (%) for C25H16N2O4S2: C, 63.10; H, 4.24; N, 16.84; S, 17.82. Found: C, 63.20; H, 4.24; N, 16.84; S, 17.82.

2.1.6 Synthesis of chromeno[2,3-d]pyrimidine derivatives (7, 8)

A solution of chromene 1 (2.8 g, 10 mmol) in ethanol (20 mL) and urea (0.6 g, 10 mmol) or thiourea (0.76 g, 10 mmol) in each case, in the presence of sodium ethoxide heated under reflux for 8 h. The reaction mixture poured onto ice/HC1, then, filtered and recrystallized from ethanol.

4-Amino-8-hydroxy-5-(4-hydroxyphenyl)-1H-chromeno[2,3-d]pyrimidine-2(5H)-thione (8)

Brown solid; yield (60%), mp 127-132°C. IR (v/cm⁻¹): 3487, 3402 (OH), 3363, 3354 (NH2), 3254 (NH); 1H NMR (DMSO-d6): δ: 4.71 (s, 1H, CH-4 pyran), 7.20-8.40 (m, 9H, ArH and NH2), 9.09 (s, 1H, OH), 9.60 (s, 1H, OH), 11.00 (s, 1H, NH). MS (m/z, %): (324, 100). Anal. Calcd. (%) for C17H13N3O3: 323.30: C, 63.16; H, 4.05; N, 13.00. Found: C, 62.94; H, 3.91; N, 12.78.

4-Amino-8-hydroxy-5-(4-hydroxyphenyl)-1H-chromeno[2,3-d]pyrimidine-2(5H)-thione (8)

Green solid; yield (60%), mp 184-186°C. IR (v/cm⁻¹): 3487, 3404 (OH), 3366, 3352 (NH2), 3262 (NH); 1H NMR (DMSO-d6): δ: 4.69 (s, 1H, CH-4 pyran), 7.20-8.40 (m, 9H, ArH and NH2), 9.11 (s, 1H, OH), 9.52 (s, 1H, OH), 10.78 (s, 1H, NH). MS (m/z, %): (340, 80.77). Anal. Calcd. (%) for C17H13N3O3S: 339.37: C, 60.17; H, 3.86; N, 12.38; S, 9.45. Found: C, 60.38; H, 4.09; N, 12.07; S, 9.29.

2.1.7 Synthesis of 1-(4-amino-8-hydroxy-5-(4-hydroxyphenyl)-2-methyl-5H-chromeno[2,3-b]pyridine-3-yl)ethanone (9)

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N-(3-Cyano-7-hydroxy-4-(4-hydroxyphenyl)-1H-chromen-2-yl) stearamide (10)

Brawn crystals yield (72%), m.p. 178-180°C. IR: 3455, 3420 (OH), 3368 (NH), 2915-2848 (CH aliphatic), 1678 (CO) and 2226 (CN); 1H NMR (CDCl3): δ 0.88 (t, 3H, CH3), 1.31-1.65 (s, 32H, CH2), 4.46 (s, 1H, CH), 7.19-8.51 (m, 8H, ArH and CH of pyrimidine), 9.35 (s, 2H, 2OH). Anal. Calcd. (%) for C34H43N3O4S: C, 73.14; H, 8.07; N, 4.87. Found: C, 73.32; H, 8.25; N, 4.63.

8-Hydroxy-5-(4-hydroxyphenyl)-3-stearoyl-1H-chromeno[2,3-d]pyrimidin-4(5H)-one (13)

Brawn solid; yield (70%), m.p. 147-150°C. IR: 3396, 3380 (OH), 2916-2850 (CH aliphatic), 1678, 1654 (CO), 1611 (C = N); 1H NMR (CDCl3): δ 0.88 (t, 3H, CH3), 1.19-1.54 (s, 32H, CH2), 3.84 (s, 1H, CH), 7.26-7.79 (m, 8H, ArH and CH of pyrimidine), 9.34 (s, 2H, 2OH). Anal. Calcd. (%) for C34H43N3O4S: C, 73.14; H, 8.07, N, 4.87. Found: C, 73.32, H, 8.25, N, 4.63.

2.2 Formation of surface active agents (19-27) from the synthesized compounds (10-18)

Addition of propylene oxide (5 moles) to the synthesized compounds (10-18) (0.1 mol) in each case, in the presence of KOH as catalyst according to\textsuperscript{30}. The amount of propylene oxide which allowed reacting, measured through the increment in mass of the reaction mixture. The addition of propylene oxide gave mixture of propoxylated products (19-27) which, confirmed based on the IR and 1H NMR spectra. Where, the IR-spectra revealed a broad band in the region of (3500-2500) cm\textsuperscript{-1} (OH) and other bands in the region of (1100-1000) and (950-900) cm\textsuperscript{-1} due to (C-O-C ether linkage of polypropoxy chain) besides the original bands. While, the 1H NMR-spectra showed a multiple signals in the region of (3.16-3.91) due to the propoxy groups in addition to the other signals of the compounds.

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2.3 Determination of the performance properties of the surface active agents (19-27)

2.3.1 Surface and interfacial tension

Surface and interfacial tension measurements for compounds (19-27) (0.1 mol/L) carried out according to Findlay (31) with a Krüss tensiometer (Krüss GmbH, Hamburg, Instrument Nr. K6) using a platinum ring at constant temperature (25°C). Paraffin oil used for the interfacial tension measurements. The tensiometer calibrated using the method described in ASTM Designation: D1331-01 (32).

2.3.2 Cloud point

Cloud point determined by gradually heating of the surfactant solution (1.0 wt%) in a bath controlled of the temperature at which the clear, or nearly clear solutions become definitely turbid. The reproducibility of this temperature checked by cooling the solutions until they become clear again (33).

2.3.3 Wetting time

The wetting time Determined by immersing a sample of cotton fabric in 1.0 wt% aqueous solution of surfactants according to Durham (33).

2.3.4 Foaming properties

The foam height measured by shaken the solution of a sample (10 mL, 20 mmol) and toluene (5 mL) at 40°C. The solution allowed to stand for 30 seconds, then, recorded the foam height (34).

2.3.5 Emulsification stability

Emulsification stability detected by shaking the aqueous solution of a sample (10 mL, 20 mmol) and toluene (5 mL) at 40°C. The emulsion stability determined as the time that took 9 mL of aqueous layer into separate from the emulsion counting since cession of shaking (35).

2.4 Biodegradability

The biodegradation tests of the synthesized nonionic surfactants were performed according to the river water Die-Away method (36). The river water for testing was sampled from the River Nile. In this test, a stirred solution containing the tested surfactant (1,000 ppm) was incubated at 25°C. Samples were withdrawn daily, filtered using Whatman filter paper and the surface tension measured using a Du-Nouy tensiometer (Krüss type K6). The process was repeated for 7 days. The biodegradation percentage D% calculated in terms of the measured surface tension according to the following relation: 

\[ D = \left( \frac{\gamma(t) - \gamma_0}{\gamma(t) - \gamma(0)} \right) \times 100, \]

where \( \gamma(t) \) = surface tension at time \( t \), \( \gamma_0 \) = surface tension at zero time, \( \gamma(t) \) = surface tension of blank experiment at time \( t \) (without samples).

2.5 Antimicrobial activity

Antibacterial and antifungal activity of the newly surface active agents investigated in vitro using cap-assay method (37) against Gram-positive bacteria (Staphylococcus aureus, Bacillus subtilis, Bacillus cereus), Gram-negative bacteria (Pseudomonas aeruginosa, Echerichia coli, Enterobacter aerogenes), as well as fungi (Aspergillus niger, Penicillium italicum, Fusarium oxysporum). In addition, a comparison between the activity of the synthesized compounds and sulphadiazine as standard drug.

3 RESULTS AND DISCUSSION

3.1 Synthesis

2-Amino-7-hydroxy-4-(4-hydroxyphenyl)-4H-chromeno-3-carbonitrile (1) prepared according to the reported procedure in literature (38), and it was turned out to be very receptive towards different reagents, to constructing phenol compounds bringing about the development of an extensive variety of annulated chromenopyrimidine systems. The cyano and amino groups provides a rich opportunity for heterocyclic construction. Thus, chromene 1 reacted with malononitrile and gave 2-(4-amino-8-hydroxy-5-(4-hydroxyphenyl)-5H-chromeno[2,3-d]pyrimidin-2-yl) acetonitrile (2).

Also, treatment of chromone 1 and excess formamide furnished 4-amino-5-(4-hydroxy-phenyl)-5H-chromeno[2,3-d]pyrimidin-8-ol (3) in good yield. The IR spectrum of 3 devoid of an absorption band for the cyano group but showed two bands for an amino group at 3372 and 3386 cm\(^{-1}\) that confirm that cyano group involved in the cyclization reaction. In contrast, cyclocondensation of chromone 1 with hot formic acid resulted 8-hydroxy-5-(4-hydroxyphenyl)-3H-chromeno[2,3-d]pyrimidin-4(5H)-one (4). The IR spectrum of 4 demonstrated a representative CO extending at 1654 cm\(^{-1}\) and the absence of any peak in the district 2000-2250 for CN group which show that CN group was included in the reaction.

The interaction between phenyl isothiocyanate and chromone 1 led to the formation of 8-hydroxy-5-(4-hydroxyphenyl)-4-imino-3-phenyl-3,4-dihydro-1H-chromeno[2,3-d]pyrimidine-2(5H)-thione (5 (Scheme 1)). The element test of 5 showed the presence of sulfur in the structure, and the IR spectrum showed the absence of peaks in the region of 2000-2250 cm\(^{-1}\), for CN group, which confirm that the cyano group involved in the reaction. Also the presence of peak in the region of 1332 cm\(^{-1}\) corresponding to thione groups. In addition, the reaction of chromone 1 with carbon disulphide in the presence of KOH afforded 8-hydroxy-5-(4-hydroxyphenyl)-1H-chromeno[2,3-d]pyrimidine-2,4(3H,5H)-dithione (6).

Quite similar chemistry involved in the formation of 4-amino-8-hydroxy-5-(4-hydroxyphenyl)-1H-chromeno[2,3-d]pyrimidin-2(5H)-one (7) or 4-amino-8-hydroxy-5-(4-hydroxy-phenyl)-1H-chromeno[2,3-d]pyrimidin-2(5H)-thione (8), by reaction of chromone 1 with urea and/or thiourea. The IR spectrum reveal that the absence of any absorption band in the region of 2150-2250 cm\(^{-1}\) for
CN group, which confirms that cyano group was involved in a cycloaddition reaction. Moreover, treatment of chromone 1 with acetyl acetone produced 1-(4-amino-8-hydroxy-5-(4-hydroxyphenyl)-2-methyl-5H-chromeno[2,3-b]pyridin-3-yl)ethan-1-one (9) (Scheme 2).

The formation of 9 can be explained by condensation of acetyl acetone with NH₂ group in compound 1 followed by the addition of an active methylene group to the CN group forming the final product 9.

3.2 Acylation of the chromenopyrimidine derivatives (1-9)

Further the compounds have been exploited to construct a chromene ring linked to fatty acid. Thus, condensation of chromene derivatives (1-9) with stearoyl chloride in the presence of triethylamine yielded the products (10-18) (Schemes 3 and 4). The structure of these compounds considered and identified from their elemental analysis, IR and ¹H NMR spectra. Where, the IR spectra displayed in the region of (2950-2514) cm⁻¹ for (CH-aliphatic), beside the original bands. While, the ¹H NMR spectra established the protons of alkyl chain, which performed as a multiple signals in the region of (1.14-1.75), besides to the other signals.

3.3 Preparation of surface active agents (19-27)

The surface active agents have a variety applications in the home and in industry due to their enough foaming and great detergency which, utilized in a variability of ways in leather industry. In order to investigate the synthesized compounds as the surface active agents, two requirements are needed to presence of suitable molecular weight to have an amphiphilic molecule with the suitable hydrophil-
ic-lipophilic balance and presence of active hydrogen atom to react with alkylene oxide. Thus, the reaction of alkylated compounds (10-18) with number of moles of propylene oxide (5 moles) in presence of KOH as a catalyst affords the corresponding propoxylated products (19-27) (Schemes 5 and 6). The reaction conditions are illustrated in Table 1.

3.4 Evaluation of surface active agents (19-27)

The construction of surface active molecules bearing heterocyclic moiety considered as an important class of organic compounds due to their double characters, one is due to disagreement between the hydrophobic and hydrophilic structure that gave surface active properties and other one due to heterocyclic moiety confirmed with aid of hydrophilic moiety (propylene oxide) that gave biological
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The surface properties includes, surface and interfacial tension, cloud point, wetting time, foaming, and emulsification properties are given in Table 2.

The obtained results indicated that the synthesized products have prominent surface activity, where, the synthesized products showed a high cloud points and good performance in hot water which, can be use at a high temperatures. Also, the prepared compounds showed a decrease of the wetting time, where, the products with effective wetting agents can find a wide application in house hold detergents and in the textile industry. In addition, the results obtained in this work revealed that, the tested compounds exhibited a low foam, where, the low foaming power compounds have some obvious application in the dyeing and auxiliary industries. Moreover, the prepared surfactants showed a good emulsifying properties which, 

Scheme 5 Propoxylation of compounds (10-14).

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can be useful in dye baths in the textile industry and emulsion paints. On the other hand, the biodegradability data were given in Table 3, within the experimental accuracy; all the prepared surfactants seem to degrade easy which means that these compounds are safe for human beings as well as environments.

3.5 Antimicrobial activity
As a part of our study about the effect of the synthesized chromene derivatives on the microbes (bacteria & fungi). Also, the effect of construction of other heterocyclic ring condensed to the chromene ring on the biological activity against bacteria and fungi was discussed. The results are listed in Tables 4 and 5. It should be noted that, since the studied compounds share the same hydrophobic (C₁₈) and the hydrophilic structure (propylene oxide) but the difference in their structures for hetercyclic moieties as chromene 19, chromenopyrimidine (20-26) and chromene-
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Table 1  Reaction conditions of propoxylated compounds (19-27).

| Compounds | Catalyst | Temperature °C | Propoxylated products | Yield % | Degree of propoxylation* |
|-----------|----------|-----------------|------------------------|---------|--------------------------|
| 10        |          |                 | 19                     | 82      |                          |
| 11        |          |                 | 20                     | 78      |                          |
| 12        |          |                 | 21                     | 80      |                          |
| 13        |          |                 | 22                     | 75      |                          |
| 14        | KOH, 0.01 wt % | 240-250      | 23                     | 79      | 5 moles                  |
| 15        |          |                 | 24                     | 83      |                          |
| 16        |          |                 | 25                     | 81      |                          |
| 17        |          |                 | 26                     | 77      |                          |
| 18        |          |                 | 27                     | 76      |                          |

* Degree of propoxylation calculated by weight.

Table 2  Surface properties of the surface active agents.

| Compounds | Surface tension (dyne/cm) 0.1 m/l | Interfacial tension (dyne/cm) 0.1 m/l | Cloud Point °C | Wetting time (sec.) | Emulsion stability (min.) | Foam height (mm) |
|-----------|-----------------------------------|----------------------------------------|----------------|--------------------|---------------------------|-----------------|
| 19        | 36                                | 12                                     | > 100          | 72                 | 100                       | 12              |
| 20        | 38                                | 15                                     | > 100          | 75                 | 135                       | 25              |
| 21        | 37                                | 11                                     | > 100          | 78                 | 125                       | 28              |
| 22        | 41                                | 17                                     | > 100          | 66                 | 130                       | 15              |
| 23        | 39                                | 16                                     | > 100          | 64                 | 140                       | 22              |
| 24        | 37                                | 11.5                                   | > 100          | 70                 | 142                       | 18              |
| 25        | 38                                | 12                                     | > 100          | 65                 | 132                       | 22              |
| 26        | 42                                | 18                                     | > 100          | 69                 | 135                       | 19              |
| 27        | 36                                | 11                                     | > 100          | 68                 | 128                       | 20              |

Error of measurements was: Surface and interfacial tensions = ± 0.1 dynes/cm. Cloud point = ± 1°C. Foam height = ± 2 mm., Wetting time = ± 1 sec., Emulsion = ± 1 min

Table 3  Biodegradability of the surface active agents (%).

| Compounds | 1st Day | 2nd Day | 3rd Day | 4th Day | 5th Day | 6th Day | 7th Day |
|-----------|---------|---------|---------|---------|---------|---------|---------|
| 19        | 40      | 48      | 59      | 70      | 83      | 92      | -       |
| 20        | 42      | 47      | 55      | 67      | 77      | 89      | 96      |
| 21        | 41      | 47      | 58      | 72      | 83      | 90      | -       |
| 22        | 45      | 52      | 64      | 76      | 88      | 92      | -       |
| 23        | 43      | 50      | 64      | 78      | 85      | 90      | -       |
| 24        | 42      | 48      | 62      | 77      | 85      | 94      | -       |
| 25        | 40      | 49      | 60      | 75      | 86      | 93      | -       |
| 26        | 47      | 55      | 66      | 79      | 89      | -       | -       |
| 27        | 41      | 46      | 56      | 68      | 79      | 86      | 95      |

Error of calculations was: Biodegradation rate = ± 0.5%
pyridine 27 which containing the phenyl (Ph), nitrile (CN), carbonyl (C=O) and/or thione (C=S) groups as function groups. So, it can be deduced that the specific skeletons in their structures are responsible for the antibacterial and antifungal activities.

Therefore, the results recorded Table 4, revealed that some of the synthesized compounds showed antibacterial activity. However, concerning the activity against Gram positive bacteria, chromenopyrimidine derivatives 23, 24 exhibited high activity, while, chromene 19 and chromenopyrimidine 26 showed moderate activity, whereas chromenopyrimidine 21 and chromenopyridine 27 showed slightly activity. On the other hand, the Gram-negative bacteria showed high responses for chromenopyrimidine derivatives 23, 24. Concerning the data of antifungal activity in Table 5. We noticed that, the chromenopyrimidine derivatives 23, 24 exposed highly responses for antifungal activity. Moreover, while chromene 19 and chromenopyrimidine 20, 26 exhibited good activity. Generally, chromenopyrimidine derivatives 23, 24 are considered to be the most active compounds in this series as they have excellent activity against both bacteria & fungi strains.

### Table 4  Antibacterial activity of the surface active agents (19-27).

| Compounds | Staphylococcus aureus | Bacillus cereus | Bacillus subtilis | Enterobacter aerogenes | Echerichia coli | Pseudomonas aeruginosa |
|-----------|-----------------------|----------------|------------------|------------------------|----------------|------------------------|
| Sulphadiazine | ++                   | ++             | ++               | +++                    | ++             | ++                     |
| 19        | +                     | +              | ++               | ++                     | +              | +                      |
| 20        | –                     | –              | +                | +                      | ++             | ++                     |
| 21        | +                     | +              | +                | –                      | –              | –                      |
| 22        | –                     | +              | ++               | –                      | +              | –                      |
| 23        | ++                    | ++             | ++               | ++                     | ++             | +++                    |
| 24        | ++                    | ++             | +++              | +++                    | +              | +++                    |
| 25        | –                     | +              | –                | +                      | –              | –                      |
| 26        | ++                    | ++             | +                | +                      | ++             | +                      |
| 27        | +                     | +              | +                | +                      | ++             | +                      |

(+++) Highly sensitive (21–25 mm); (++) Fairly sensitive (16–20 mm); (+) Slightly sensitive (10–15 mm); (–) Not sensitive.

### Table 5  Antifungal activity of the surface active agents (19-27).

| Compds. | Aspergillus niger | Penicillium italicum | Fusarium oxysporum |
|---------|-------------------|----------------------|--------------------|
| Sulphadiazine | ++               | ++                   | ++                 |
| 19      | ++                | +                    | +                  |
| 20      | ++                | +                    | +                  |
| 21      | +                 | +                    | +                  |
| 22      | +                 | +                    | +                  |
| 23      | ++                | +                    | ++                 |
| 24      | ++                | ++                   | ++                 |
| 25      | +                 | +                    | +                  |
| 26      | +                 | +                    | +                  |
| 27      | +                 | +                    | –                  |

Highly sensitive (+++); Fairly sensitive (++); Slightly sensitive (+); Not sensitive (–).

4 CONCLUSION

This study reports the successful synthesis and surface active of chromenopyrimidine derivatives linked to fatty chain. It can be concluded that the produced nonionic surface active agents (19-27) exhibited emulsion characteristics. Where a lot of textile procedures such as washing and coloring, it is needed to enter the surfactants into the wash to remove the oily impurities from the fibers. Thus, the possibility of their use in the media, non-edible, such as
insecticides or pesticides, as well as in the pharmaceutical and cosmetics industry.

5 ACKNOWLEDGEMENT

The authors would like to thank the staff of the Faculty of Science, Microbiology Department, Umm Al-Qura University for biological activity screening of the tested compounds. Also, express our indebtedness and deepest gratitude to Dr. D. E. Ghaful, for his helping throughout this work.

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