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Synthesis and characterization of coumarin thiazole derivative 2-(2-amino-1,3-thiazol-4-yl)-3*H*-benzo[*f*]chromen-3-one with anti-microbial activity and its potential application in antimicrobial polyurethane coating

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ABSTRACT

Coumarin, thiazole and their respective derivative products are some of the oldest and most commonly known class of nitrogen and sulphur containing compounds. In recent years there has been considerable interest in this coumarin–thiazole derivatives, which have been reported to exhibit significant biological activity and are widely used as pharmaceuticals. They are capable of imparting anti-microbial activity properties when incorporated into polymers and polymer composites. In this research, coumarin–thiazole derivative 2-(2-amino-1,3-thiazol-4-yl)-3*H* benzo[*f*]chromen-3-one (compound III), was prepared and its structure was confirmed by means of its spectra data. It was also screened for its anti-microbial activity against eight different micro-organisms when physically incorporated into a polyurethane varnish formula. Experimental coatings were manufactured on a laboratory scale and applied by means of a brush on both glass and steel panels. The results of the biological activity indicated that the polyurethane varnishes containing the 2-(2-amino-1,3-thiazol-4-yl)-3*H*-benzo[*f*]chromen-3-one (compound III) derivative, exhibit a very good antimicrobial effect. The molecular modeling study revealed that it is biologically safe, it is active and it fulfills Lipinski's rule of five. The physical and mechanical resistances of the polyurethane varnish formulations were also studied to evaluate any drawbacks associated with the addition of the derivative. The studies indicate that the physical incorporation of compound III actually enhances slightly both the physical and mechanical properties.

1. Introduction

Polyurethane's are an important and versatile class of polymer, they are susceptible to microbial attack when they are exposed to atmosphere, or used as an adhesive or a coating material [1–4]. Generally micro-organisms have been found to cause disbonding and blistering of coatings under various service conditions [5–7]. Marine bio-fouling is a natural phenomenon representing one of the greatest problems in marine technology and navigation. This is due to the accumulation of organisms such as barnacle, tube worms and algae on the submerged surfaces of the vessels, which result in important speed reduction and considerably higher fuel consumption. To circumvent these problems, antifouling paints, i.e. paint formulations traditionally containing biocidal species, are used to protect the submerged surfaces from marine bio-fouling [8]. Up until the end of 1990s, the most effective anti-fouling paints were based on organotin compounds, mostly tributyltin compounds (TBT-based paints). TBT and its derivatives were found to be harmful molecules to marine eco-systems by Alzieu [9]. Thus, TBT-based paints were completely prohibited by 1 January 2008 [10,11] and as a consequence promoted research into new ecological paints. One possibility following the prohibition was to develop polymers having biocidal activities [12]. A large number of naturally occurring compounds contain heterocyclic rings as a key part of their structure e.g. coumarin (IUPAC name: *2H*-Chromen-2-one) compounds and its derivatives, and these are used as medicines [13]. Coumarin

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compounds and their derivatives form a group of more than forty drugs, which are widely used in medicine as anticoagulant, hypertensive, antiarrhythmic, immunomodulant agents, and they possess remarkable activities against bacteria [14] and fungi [15]. Furthermore, coumarin derivatives having various substituted thiazole rings at carbon-3 exhibit promising biological activities. The chemistry of couramin derivatives continues to draw the attention of synthetic organic chemists due to their varied biological activities [16,17]. Compounds containing thiazole rings are also a familiar group of heterocyclic compounds possessing a wide variety of biological activities and have a remarkable medicinal value, due to their potential chemo-therapeutic properties. The thiazole nucleus is also an integral part of all the available penicillins, which have revolutionized the therapy of bacterial diseases. Thiazoles have attracted continued interest due to their varied biological activities [18], which have found applications in the treatment of microbial infections [19,20]. Thiazole is a parent material for various chemical compounds including sulfur drugs, biocides, fungicides, dyes, and chemical reaction accelerators. In addition, 2-amino thiazole derivatives are reported to exhibit significant biological activities and are widely used as pharmaceuticals. Coumarin thiazol analogs have been found to have potential as anti-cancer and anti-microbial agents [21]. On the basis of all of this evidence, this study reports the synthesis, characterization and anti-microbial activities of new structure hybrids, incorporating the coumarin and thiazole ring system. This combination was anticipated to have an influence on the biological activities. The coumarin thiazole derivative 2-(2-amino-1,3-thiazol-4-yl)-3*H*-benzo[*f*]chromen-3-one (compound III), was physically added to the polyurethane varnish, to make it anti-microbial. The biological activity test was used to assess the biological activity influence of the additive. The physical resistance and mechanical resistance were also studied to evaluate any drawbacks associated with the additive.

2. Experimental

2.1. Materials

All the chemicals used during the research project were sourced internationally, or from local companies, and were of pure grade quality.

2.2. Methods and techniques

The coumarin thiazole derivative 2-(2-amino-1,3-thiazol-4-yl)-3*H*-benzo[*f*]chromen-3-one (compound III) was prepared in three steps as presented in Scheme 1 and as described below.

2.2.1. Synthesis of 2-acetyl-3H-benzo[f]chromen-3-one (compound I)

In a 250 ml three-neck round bottom flask, a mixture of 2-hydroxy-1-naphthaldehyde (0.1 mol, 17.2 g) and ethyl acetoacetate (0.1 mol, 13 g) was added to 50 ml of ethanol. Piperidine was used as the catalyst, with 3–4 drops being added to the reaction mixture, prior to the reaction mixture being stirred for 10 min at room temperature. The reaction mixture was then further heated for 2 h in a water bath. A yellow solid was obtained and this was separated by filtration, then washed with cold ether and then dried over the vacuum pump. The material was then re-crystallized from a chloroform/hexane solvent mixture according to the literature procedure [22,23].

2.2.2. Synthesis of 2-(bromoacetyl)-3H-benzo[f]chromen-3-one (compound II)

2-Acetyl-3*H*-benzo[*f*]chromen-3-one (compound I) (0.01 mol, 2.38 g) was stirred in 30 ml acetic acid, with the bromine (0.01 mol) being added drop-wise. After the addition of the bromine, the reaction mixture was left over a 60 min period. The reaction mixture was then poured into 100 ml of cold water, and the solid obtained was filtered and re-crystallized from benzene [24].

Table 1
Composition of the polyurethane varnish studied.

Component	wt%
Refined sunflower oil	33.42
Glycerol	0.039
Litharge (lead oxide catalyst)	0.03
Pentaerythritol	4.61
Turpentine	47.33
Barium octoate drier	0.26
Toluene diisocyanate	11.37
Mixed drier	2.11
UV absorber	0.26
Anti skinning agent	0.32
Biocide (compound III) additive	0.1,0.5,1.0

Properties: viscosity: G-I (gardner); color: 3 (gardner); solid content: 53 ± 2%.

2.2.3. Synthesis of coumarin thiazole derivative 2-(2-amino-1,3-thiazol-4-yl)-3H-benzo[f]chromen-3-one (compound III)

A mixture of 2-(bromoacetyl)-3*H*-benzo[*f*]chromen-3-one (compound II) (0.01 mol, 3.17 g) and thiourea (0.01 mol, 0.76 g) was dissolved in 30 ml absolute ethanol. The reaction mixture was then refluxed for 2 h. A precipitate formed on cooling, which was collected by means of filtration, washed with ethanol and dried under vacuum. The solid obtained was then re-crystallized with an ethanol/benzene solvent mixture, resulting in brown–colored crystals.

2.3. Characterization studies

Melting points for the three compounds were determined with a Stuart Scientific Company melting point apparatus. Elemental analysis was performed using a Perkin-Elmer 240 micro-analyzer at the Micro-Analytical Center of Cairo University. The IR spectra were recorded using an FT-IR 5300 spectrophotometer and ^{1}H NMR spectra ($CDCl_3$) recorded on a Varian Gemini 300 MHz spectrometer and chemical shifts were expressed in δ ppm units, using TMS as an internal standard.

2.4. Preparation of antimicrobial (biocidal) coating

To fully understand the anti-microbial activity of coumarin thiazole derivative 2-(2-amino-1,3-thiazol-4-yl)-3*H*-benzo[*f*]chromen-3-one (compound III), it was incorporated into a commercial polyurethane varnish at the levels of 0.1, 0.5 and 1.0%. The composition of the polyurethane varnish used for the study is tabulated in Table 1. The samples of different molar ratio were then applied to both glass and steel panels by means of a brush. All efforts were made to maintain a uniform film thickness of 50 ± 5 μm for evaluating the physical and mechanical properties.

2.5. Antimicrobial screening

The anti-microbial activity of the synthesized coumarin thiazole derivative 2-(2-amino-1,3-thiazol-4-yl)-3*H*-benzo[*f*]chromen-3-one(compound III) was tested against eight different micro-organisms namely, Gram-negative bacteria(G−) *Escherichia coli* (*E. coli*) and Salmonella, Gram-positive bacteria(G+) *Micrococcus luteus* (*M. luteus*), and *Staphylococcus aureus* (*S. aureus*), and *Aspergillus flower* (*A. flower*), *Penicillium citricus*, *Candida albicans* and Suserium for fungi. Nutrient agar was used as the medium.