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Synthesis and evaluation of antibacterial and antibiofilm activities of pyridin-2-yl hexanoate

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ABSTRACT

Synthesized Pyridin-2-yl hexanoate was screened for its antibacterial and antibiofilm activities using the broth microdilution method and XTT assay respectively. The obtained results revealed that synthesized molecule inhibited the growth of pathogenic bacteria (MICs value ranged from 80 to 640 μg ml^{-1}). Moreover, it induced a strong antibiofilm effect against Gram positive cocci (BIC_{50} was 366, 378 and 412 μg ml^{-1} for *Streptococcus mutans* ATCC 25175, *Streptococcus salivarius* ATCC 13419 and *Streptococcus oralis* ATCC 6249 respectively). Basis on these results, pyridin-2-yl hexanoate may be considered as effective compound with antibacterial and antibiofilm activities.

1. Introduction

The nitrogen heterocyclic skeleton is the main source of many important pharmaceuticals and physiologically active products. The heterocyclic compounds continue to be attractive for synthesis since they exhibit biological properties [1–3]. Pyridin-2(1H)-ones are compounds with antibacterial, antifungal, antiviral, anti-malarial, anti-inflammatory, and anti-tumoral activities [4–6]. Moreover, pyridin-2(1H)-ones have been used as an intermediate in a pyridine, quinolizidine, and indolizidine alkaloids synthesis process [7]. Heterocycles containing an acyl group are of importance for making new pharmacological compounds [8,9].

It has been reported that bacteria embedded in biofilm are more resistant to conventional drugs [10]. Antibiofilm property of synthetic compound has been studied elsewhere [11–13]. Ishida et al. [14], noticed that N-acyle cyclopentylamides inhibit the quorum sensing and biofilm formation of *Pseudomonas aeruginosa*. Additionally, 3,4,5,3′,5′-pentabromo-2-(2′-hydroxybenzoyl) pyrrole, a synthetic anti-bacterial compound related to pyrrolomycins, was active at low concentrations against preformed *Staphylococcus epidermidis* and *Staphylococcus aureus* biofilms [13]. More recently, Mohammad et al. [15], reported that thiazole derivative may reduce *S. epidermidis* biofilm. In the same field, Dragovich et al. [16], demonstrated the antiviral activity of bicyclic 2-pyridone-containing compound (82) on human rhinovirus serotypes (EC50: from 0.037 to 0.162 mM).

The present investigation deals in developing an effective approach to synthesize pyridin-2-yl hexanoate compound. Then the synthesized compound was evaluated for its antibacterial and antibiofilm activities.

2. Material and methods

2.1. Pyridin-2-yl hexanoate synthesis

A 500 mg, (5.5 mmol) of 2-hydroxypyridine was dissolved in 3 mL dimethylformamide (DMF), then hexanoylchloride (5.5 mmol) was added and the resulting mixture was stirred at room temperature overnight. Twenty ml of water was added, then the mixture was extracted with CH_2Cl_2 (50 mL × 3), and the organic layer was washed with water (50 mL), dried over Na_2SO_4 and concentrated in vacuum to afford the products (99%).

IR ύ = 1713 cm^{-1}(C═O), 1652 cm^{-1} (C═N), 1619 cm^{-1} (C═C), ^{1}H NMR (600 MHz, DMSO) δ = 7.43–7.39 (m, 1H), 7.38–7.32 (m, 1H),

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Table 1
Antibacterial activity of pyridin-2-yl hexanoate against oral bacteria.

Strains	Antimicrobial susceptibility					
	[a]TET (μg.mL^{-1})		[b]CHX (μg.mL^{-1})		pyridin-2-yl hexanoate (μg.mL^{-1})	
	[c]MIC	[d]MBC	MIC	MBC	MIC	MBC
Streptococcus mutans ATCC 25175	2	4	4	8	80	160
Streptococcus oralis ATCC 6249	4	8	8	16	80	320
Streptococcus salivarius ATCC 13419	8	8	16	16	80	160
Lactobacillus plantarum ATCC 8014	32	32	8	8	640	1280
Enterococcus faecalis ATCC 29212	64	64	256	256	320	640
Staphylococcus aureus ATCC 25923	8	32	32	64	320	320
Micrococcus luteus ATCC 10240	16	32	16	16	160	160
Esherichia coli ATCC 25922	64	128	32	64	640	640

[a] Tetracycline.
[b] Chlorhexidine digluconate.
[c] Minimum inhibitory concentration.
[d] Minimum bactericidal concentration.

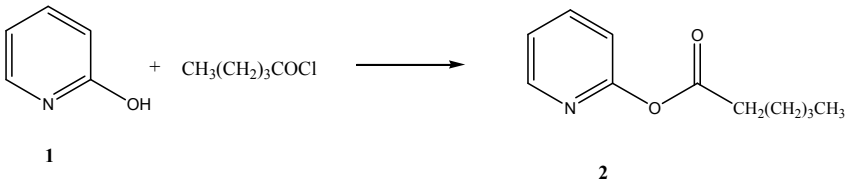

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Fig. 1. Synthesis of pyridin-2-yl hexanoate.

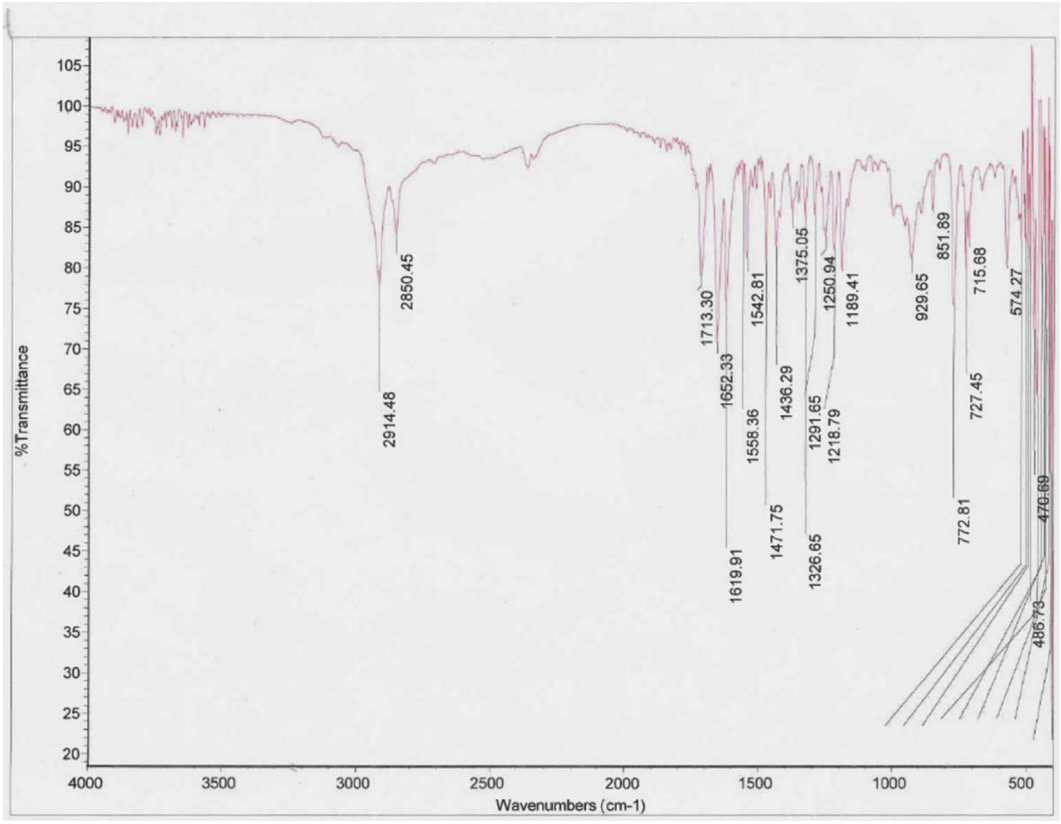

Fig. 2. IR spectra of synthetisis Pyridin-2-yl hexanoate.

6.34 (d, J = 9.2 Hz, 1H), 6.18–6.15 (m, 1H), 2.4 (t, J = 7.5 Hz, 2H), 1.68–1.52 (m, 2H), 1.32–1.15 (m, 24H), 0.89 (m, 3H).

2.2. In vitro antibacterial activity

In this study, 8 reference strains (Table 1) were used to evaluate pyridin-2-yl hexanoate antimicrobial activity using the broth microdilution method. Serial two-fold dilutions of tetracycline (0–512 μg mL^{-1}), chlorhexidine digluconate (Sigma-Aldrich, Switzerland) (0–512 μg mL^{-1}) and pyridin-2-yl hexanoate (0–1280 μg mL^{-1}), were prepared in Muller Hinton (MH) Broth.

The inocula (10 μL) of each strain (10^5 cfu mL^{-1}) was added to the