Egyptian Journal of Aquatic Biology & Fisheries
Zoology Department, Faculty of Science,
Ain Shams University, Cairo, Egypt.
ISSN 1110 – 6131
Vol. 26(5): 1229 – 1239 (2022)
www.ejabf.journals.ekb.eg

Antibacterial effect of rhodanine derivatives against bacteria isolated from the River Nile, Egypt

Saleh Ahmed Rabeh
National Institute of Oceanography and Fisheries, Cairo, Egypt.
dr.salehrabeh@hotmail.com

ARTICLE INFO

Article History:
Received: Oct. 15, 2022
Accepted: Oct. 27, 2022
Online: Oct. 30, 2022

Keywords:
River Nile,
Pathogenic bacteria,
Rhodanine derivatives,
Antibacterial agent

ABSTRACT

The objectives of the present study were to isolate and identify some pathogenic bacteria from the River Nile water and to evaluate the rhodanine derivatives as potent antibacterial agents.The results showed that rhodanine derivatives No. 7c and 8 were the most effective against all tested bacteria.On the other hand, rhodanine derivatives, No. 2a,2b, 2c and 9b have no antibacterial activities against pathogenic Gram-positive and Gram-negative bacteria, while the other derivatives exhibited either low or moderate antibacterial activities against some of the tested bacteria.Therefore, it was suggested that rhodanine derivatives are promising as novel antibacterial agents for pharmaceutical applications, water treatment and preventing and controlling fish diseases in aquaculture.

INTRODUCTION

Although the River Nile is the main source of fresh water in Egypt , where the Egyptians depend on it for almost 90% of its water supply, particularly in irrigation (**Ali *et al*.,2014**), it subjected to pollution through several anthropogenic activities, e.g., drainage of untreated agricultural flows, sewage and industrial wastewater.

The search for a more potent new antibacterial compounds are required to withstand the increasing number of bacterial pathogens and the growing problems of antibiotic resistance (due to excessive use of antibiotics). A large number of compounds which containheterocyclic moieties display biological activity. Their biological activity is mainly dependent on their molecular structures (**Elzahany*et al*., 2008**) and may be also related to different mechanisms of action.Rhodanine and its derivatives have attracted considerable attention in a wide range of pharmaceutical applications and water treatment (**Klerk *et al*., 2017**) due to their unique biological activities, including antimicrobial (**Arafa *et al*., 2016 a**), antibacterial (**Hardej *et al*., 2010; Song *et al*., 2012; Chao *et al*., 2015; Arafa *et al*., 2016 b**), antidiabetic (**Murugan *et al*., 2009**), antifungal (**Liaras *et al*., 2011)**, antiviral (**Foye and Tovivich**, **1977**) anticancer (**Moorthy *et al*.,2010)** and anti-inflammatory (**Won *et al*., 2005)**.

River Nile water contamination can cause waterborne outbreaks and constitute a serious health implications as result of unsafe drinking water leading to health threat for consumers, limitations on recreational activities, and aquaculture (**Rabeh *et al*., 2007;**

Sabae and Rabeh, 2007; Rabeh, 2010). Thus, attention has been directed to the synthesis and production of rhodanine derivatives as antimicrobial agents to improve thewater quality as well as preventing and controlling of fish diseases .
The aim of the present work was isolation and identification of some pathogenic bacteria from the River Nile water as well as biological evaluation of rhodanine derivatives as potent antibacterial agents to use for pharmaceutical applications, water treatment and preventing and controlling of fish diseases in aquaculture.

MATERIALS AND METHODS

Study Area

The River Nile originates in Lake Victoria as the Victorian or White Nile, which is joined in Khartoum, Sudan with the Blue Nile, springing from Lake Tana in Ethiopia. The River Nile continues to flow up northward untilit drains in the Mediterranean coast of Egypt through Damietta and Rosetta Branches both of which branch out at El-Qanater , north Cairo (**Fielding *et al*., 2018**).

In our previous work (**Arafa *et al*., 2016 b**),15 rhodanine derivatives were synthesised (Table 1).

Table (1).The synthesised rhodanine derivatives

No.	Name	Function groups
2a	ethyl (Z)-2-(3-cyclohexyl-4-oxo-2-thioxothiazolidin-5-ylidene)acetate	Rhodanine ring, cyclohexyl ring, ethyl ester group.
2b	methyl (Z)-2-(3-cyclohexyl-4-oxo-2-thioxothiazolidin-5-ylidene)acetate	Rhodanine ring, cyclohexyl ring, methyl ester group.
2c	ethyl (Z)-2-(3-isopropyl-4-oxo-2-thioxothiazolidin-5-ylidene)acetate	Rhodanine ring, isopropyl moiety, ethyl ester group.
2d	ethyl (Z)-2-(3-(sec-butyl)-4-oxo-2-thioxothiazolidin-5-ylidene)acetate	Rhodanine ring, isobutyl moiety, ethyl ester group.
2e	ethyl (Z)-2-(3-benzyl-4-oxo-2-thioxothiazolidin-5-ylidene)acetate	Rhodanine ring, benzyl moiety, ethyl ester group.
2f	ethyl (Z)-2-(3-(4-hydroxybenzyl)-4-oxo-2-thioxothiazolidin-5-ylidene)acetate	Rhodanine ring, p-hydroxybenzyl moiety, ethyl ester group.
2g	ethyl (Z)-2-(3-(4-chlorobenzyl)-4-oxo-2-thioxothiazolidin-5-ylidene)acetate	Rhodanine ring, p-chlorobenzyl moiety, ethyl ester group.
2h	ethyl (Z)-2-(3-(4-bromobenzyl)-4-oxo-2-thioxothiazolidin-5-ylidene)acetate	Rhodanine ring, p-bromobenzyl moiety, ethyl ester group.
2i	ethyl (Z)-2-(3-(4-fluorobenzyl)-4-oxo-2-thioxothiazolidin-5-ylidene)acetate	Rhodanine ring, p-fluorobenzyl moiety, ethyl ester group.
7a	3-cyclohexyl-3'-phenyl-2,2'-dithioxo-[5,5'-bithiazolidine]-4,4'-dione	Bis-rhodanine ring, cyclohexyl ring, Benzene ring
7b	3-(4-chlorophenyl)-3'-cyclohexyl-2,2'-	Bis-rhodanine ring, cyclohexyl ring,

	dithioxo-[5,5'-bithiazolidine]-4,4'-dione	p-chlorophenyl moiety
7c	3-cyclohexyl-3'-(4-methoxyphenyl)-2,2'-dithioxo-[5,5'-bithiazolidine]-4,4'-dione	Bis-rhodanine ring, cyclohexyl ring, p-methoxyphenyl moiety
8	ethyl 3-cyclohexyl-2,5-dithioxo-3,7-dihydro-2H-[1,3]oxathiino[6,5-d]thiazole-7-carboxylate	1,3-thiazole moiety,1,3-oxathiinemoiety, Cyclohexyl ring,Ethyl ester group.
9a	methyl 5-amino-6-cyano-3-cyclohexyl-2-thioxo-3,7-dihydro-2H-pyrano[2,3-d]thiazole-7-carboxylate	1,3-thiazole moiety, Pyran ring, Cyclohexyl group,methyl ester group, cyano group, amino group.
9b	ethyl 5-amino-6-cyano-3-cyclohexyl-2-thioxo-3,7-dihydro-2H-pyrano[2,3-d]thiazole-7-carboxylate	1,3-thiazole moiety, Pyran ring, Cyclohexyl group, ethyl ester group, cyano group, amino group.

Microorganisms

Nine Gram-negative and one Gram-positive bacteria were used in this investigation. Four bacteria were isolated from the River Nile water, while other identified ones were obtained from different sources and used as indicator organisms.

Identified bacteria

Erwinia herbicola 48 was identified by **El-Hendawy and Azab (1998)**, while *Bacillus subtilis* 1020 and *E. coli* 1357, were obtained from the culture collection of the Microbiological Resource Center (MIRCEN), Faculty of Agriculture, Ain-Shams University, Cairo, Egypt. *Klebsiella pneumonia* (clinical isolate) was kindly obtained from Department of Microbiology, Faculty of Pharmacy, Tanta University, Egypt, while *Proteusvulgaris* 1753 and *Serratia marscens* HIM 307-2 were kindly provided by Professor Martin, H.H, Institute of Microbiology, TH Darmstadt, Germany.

Unidentified bacteria

The unidentified bacteria were isolated from the River Nile water.

Isolation and purification of Gram-negative bacteria

Isolation of Gram-negative bacteria fromthe River Nile water were performed using MacConkey agar supplemented with 0.001 g L^{-1} crystal violet (**Rabeh and Azab,2006**) . Twenty isolates were purified, screened and the suspected similar ones were grouped for the purpose of selection and identification processes.

Identification of Gram-negative pathogens

Twenty isolates from the examined water samples were subjected to identification by using API 20E strip system (BioMereux). The inoculated strips were incubated for 16-24 h and the color reactions were recorded either positive or negative.

Antimicrobial assay

Well assay technique was used (**Holmalahti *et al*., 1994**). Bacterial overnight cultures were prepared in culture broth and diluted to 1×10^{6} cfu ml^{-1} and used for inocula.

Statistical Analysis

Statistical analysis of the obtained data was subjected to analysis of variance (ANOVA) using Microsoft Excel 2016.

RESULTS

Identification of isolated bacteria

Escherichia coli, *Salmonella enterica*, *Shigella* sp. and *Brenneria nigrifluens* were the identified G-negative bacteria (Table 2) according to the biochemical reactions of API 20E.

Table (2). Identification of Gram –negative pathogenic bacteria using API 20E

ONPG	ß-galactosidase Ortho NitroPhenyl-ßD-(Galactopyranosidase)	+	-	-	-
ADH	Arginine dihydrolase	-	-	-	-
LDC	Lysine decarboxylase	-	+	+	-
ODC	Ornithine decarboxylase	-	+	+	-
CIT	Citrate utilization	-	-	-	-
H_2S	H_2S production	-	-	-	-
URE	Urea hydrolysis	-	-	-	-
TDA	Tryptophan deaminase	-	-	-	-
IND	Indole production	+	-	-	-
VP	Voges Proskauer (Acetoin production)	-	-	-	+
GEL	Gelatinase	-	-	-	-
GLU	Glucose	+	+	+	+
MAN	Mannitol	+	+	-	+
INO	Inositol	-	-	-	-
SOR	Sorbitol	+	+	-	+
RHA	Rhamnose	+	+	-	+
SAC	Sucrose	-	--	-	+
MEL	Melibiose	+	-	-	+
AMY	Amygdalin	-	-	-	+
ARA	Arabinose	+	-	-	+
OX	Oxidase	-	-	-	-
NO_2	NO_2 Nitrate reduction to	+	+	+	+
N_2	Nitrate reduction to N_2 gas	-	-		-
MOB	Motility	+	+	-	+
McC	MacConkey medium	+	+	+	+
OF-O	OF Medium- Oxidation	+	+	+	+
OF-F	OF Medium- Fermentation	+	+	+	-
Confirmed as		*E. coli*	*Salmonella enterica*	*Shigella* sp.	*Brenneria nigrifluens*

Table (3).Inhibition zones of rhodanine derivatives against isolated test bacteria

Inhibition zone (cm)															
Derivatives Test organisms	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
E. coli	-	-	-	0.7	0.7	-	-	-	-	-	0.9	1.8	1.4	1.2	-
Salmonella enterica	-	-	-	-	-	-	0.3	0.7	0.6	0.9	0.7	1.7	1.4	0.9	-
Shigella sp.	-	-	-	-	-	-	-	-	-	-	-	1.3	1.4	0.9	-
Brenneria nigrifluens	-	-	-	-	-	-	-	-	0.7	-	0.9	1	0.7	0.5	-

Table (4). Inhibition zones of rhodanine derivatives against indicators bacteria

Inhibition zone (cm)															
Derivatives Indicator organisms	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
Bacillus subtilis 1020	-	-	-	-	-	-	-	-	-	-	-	1.8	1	-	-
Escherichia coli 1357	-	-	-	0.9	0.9	-	-	-	-	-	0.8	1.7	1.3	1.1	-
Proteus vulgaris 1753	-	-	-	-	-	-	1.5	0.8	0.8	0.8	0.9	1.8	1.8	1.7	-
Erwinia herbicola 48	-	-	-	-	-	-	-	-	-	-	0.7	1.2	0.8	0.7	-
Klebsiella pneumonia	-	-	-	1.2	-	-	0.6	-	-	-	1.0	2	1.7	0.6	-
Serratia marscens HIM 307-2	-	-	-	-	-	-	-	-	0.9	-	-	1.5	2.4	-	-

DISCUSSION

During the present investigation, G. negative bacteria *Escherichia coli, Salmonella enterica, Shigella sp,* and *Brenneria nigrifluens* were the identified. *E. coli* presence in water sample usually indicates recent faecal contamination.Pathogenic forms of *E. coli* can cause a variety of diarrhoeal diseases in hosts due to the presence of specific colonisation factors, virulence factors and pathogenicity associated genes which are generally not present in other *E. coli*; the predominant facultative organism in the human gastrointestinal tract as a subgroup of faecal coliforms. Six pathotypes of the strains that cause diarrhoeal diseases are now recognised (**Donnenberg, 2002**).The serogroups, *Salmonella enterica* (formerly *Salmonella choleraesuis*)are the most of the human pathogenic *Salmonella* which include *Salmonella Typhi*, *Salmonella Enteritidis*, *Salmonella Paratyphi*, *Salmonella Typhimurium*, and *Salmonella Choleraesuis* (**Giannella, 1996**; **Murray *et al*., 2009).**

Shigella dysenteriae, *S. boydii*, *S. flexneri* and *S. sonnei* are the pathogenic species of to humans (**Subekti *et al*., 2009.** Most members of *Brenneria* were formerly placed in *Erwinia* (**Toth *et al*., 2003**). Several species of this genus have been reclassified, and novel species added, due in part, to ongoing research on the potential involvement of *Brenneria* in acute oak decline disease in the United Kingdom (**Denman *et al*., 2014).**

The present study revealed that rhodanine derivatives No. 7c and 8 were the most effective against all tested bacteria.On the other hand, rhodanine derivatives, No. 2a,2b, 2c and 9b have no antibacterial activities against pathogenic Gram- positive and Gram-negative bacteria, while the other derivatives exhibited either low or moderate antibacterial activities against some of the tested bacteria. In accordance with our results, **Klerk, *et al*.,** (**2017**) indicated that all investigated bacteria were susceptible to the rhodanine monomer. Gram-positive bacteria were found to be more vulnerable than Gram-negative.*S. aureus* and *B. subtilis* showed inhibition zones of up to 13.75± 0.17 mm and 15.83 ± 0.51 mm, respectively. The largest clear zones for *E.coli* and *S.typhi* were determined to be 21.13 ± 0.35mm and 15.17 ± 2.12 mm diameters, respectively.

Greater understanding of the molecular structure, mechanisms of the chosen intervention targets and of the pathogenic role played by the target in the infection process is required for the prevention and treatment of bacterial infections. Bacterial infections are complex and involve the action of a large sophisticated arsenal of virulence factors, many of which are surface-bound or secreted. Gram-positive bacteria are endowed with a multitude of cell wall anchored proteins that serve as an interface between the microbe and its host. Bacterial sortases are cysteine transpeptidases that participate in secretion and anchoring of many cell wall proteins by a mechanism conserved in almost the entire class of Gram-positive bacteria (Navarre, and Schneewind, 1999, Cossart and Jonquieres , 2000).

Opperman et al (2009) found that rhodanines inhibit early phase biofilm formation by multiple strains of S. aureus, S. epidermidis, and E. faecalis.Our findings were in

agreement with previous study of **Grant *et al* (2000)** that has shown that rhodanine compounds inhibit class C b-lactamases in Gram-negative bacteria**. Zervosen *et al*. (2004)** reported that several arylalkylidene rhodanines have also been reported that have high bactericidal activity against non-resistant *S. aureus* and MRSA strains, while some rhodanines probably act on the enzyme through a thiol-disulfide exchange reaction with Cys 184 (**Suree and Thieu , 2009**).On the other hand ,**Singh *et al*.,**(**2012**) found that rhodanine compounds had a high affinity for FtsZ , inhibited its GTPase activity in vitro, FtsZ-ring formation *in vivo* and inhibited *B. subtilis* growth.The N-carboxymethyl moiety was necessary for anti-bacterial activity against Gram-positive bacteria and the inclusion of a phenmethyl moiety or other hydrophobic substituent at the N-carboxymethyl moiety was necessary to increase the antibacterial activity. Some rhodanines were reported to inhibit bacterial RNA polymerase (**Gualtieri**,***et al***.,**2006**), while others are likely to have (an) additional target(s) in Mtb besides DlaT, in particular because it accumulates in mycobacteria to very high concentrations.

Mur ligases participate in the intracellular path of bacterial peptidoglycan biosynthesis and constitute attractive, although so far underexploited, targets for antibacterial drug discovery. Some rhodanine derivatives were balanced inhibitors of Mur D, -E, and – F (**Tomasic**, ***et al*., 2009**).Moreover,the acetic acid group on the 3-position of the rhodanine was also substituted with an aliphatic side chain aiming to increase the bacterial cell wall penetration of these compounds and therefore potentially improve their antibacterial activities (**Song *et al*., 2015**).

ANOVA results indicated a relative variance between using different derivatives of rhodanine compound against isolated test bacteria (0.16 at $P < 0.05$) for the 2d, 2e, 2i and 7b ,respectively while the other ones didn't show any variance. On the other hand, *E. coli* and *Salmonella enterica*are the most bacterial species affected. However, there are considerable variance (0.32 – 0.42 at $P < 0.005$) in case of using rhodanine derivatives against indicators bacteria especially of 9a, 2g, 8 and 2d derivatives, respectively. The highest affected species was *Proteus vulgaris* 1753 followed by *Serratia marscens* HIM 30702 and *Klebsiella pneumonia* with variance of (0.53, 0.51, 0.46 at $P < 0.05$, respectively).

CONCLUSIONS

- Some rhodanine derivatives synthesized in this investigation possess *in vitro*antibacterial activity against the tested bacteria, while others had no antimicrobial activity.
- Rhodanine derivatives the No 8 appeared to be the most effective against almost all used bacteria.
- The efficiency of the rhodanine derivatives varied with, structure, and functional groups.

RECOMMENDATIONS

- As a therapy against various diseases, the effective rhodanine derivatives may be of great use for the development of pharmaceutical industries.
- Rhodanine derivatives are promising scaffolds for the development of novel antibacterial agents.
-The effective rhodanine derivatives may be used for food preservation or medicinal purposes after some experiments for safety and toxicity.
- Rhodanine derivatives are promising as novel antibacterial agents for pharmaceutical applications, water treatment and preventing and controlling of fish diseases in aquaculture.

REFERENCES

Ali, E.; Shabaan-Dessouki, S.; Soliman, A. and El Shenawy, A. (2014). Characterization of chemical water quality in the Nile River, Egypt. Int. J. Pure Appl Biosci., 2(3):35-53.

Arafa, W. A. A. ; Fareed, M. F.; Rabeh S. A.and Shaker, R. M.(2016a). Ultrasound Mediated Green Synthesis of Rhodanine Derivatives: Synthesis, Chemical Behavior and Antibacterial Activity. Phosphorus, Sulfur, and Silicon and the Related Elements,191:1129-1136.

Arafa, W. A. A. ; Shaker R. M.and Rabeh,S. A.(2016b).Prospective study directed to the synthesis of symmetrical linked bis-rhodanine derivatives with their antimicrobial activity. Heterocycles, 92: 1224- 1243.

Chao, L.; Jia-Chun,L.; Ya-Ru,L.; Cheng, G.; Mei-Ling,Z.; Hong-Yan, L.; Xiao-Zhen,L.; Chang-Ji,Z.and Hu-Ri, P. (2015). Synthesis and antimicrobial evaluation of 5-aryl-1,2,4-triazole-3-thione derivatives containing a rhodanine moiety. Bioorg. Med. Chem. Lett., 25: 3052-3056.

Clubb,R.T.(2009).Discovery and structure-activity relationship analysis of *Staphylococcus aureus* sortase A inhibitors.Bioorg Med Chem., 17(20):7174-7185.

Cossart, P. and Jonquieres,R.(2000). Sortase, a universal target for therapeutic agents against gram-positive bacteria?. Proc. Natl. Acad. Sci. U S A., 97: 5013-5015.

Denman, S.; Brown , N .; Kirk , S .; Jeger, M . and Webber,J.(2014). A description of the symptoms of Acute Oak Decline in Britain and a comparative review on causes of similar disorders on oak in Europe. Forestry, 87: 535–551.

Donnenberg, M. S. (2002). Introduction pp. I In Donnenberg, M.S. (Ed.) *Escherichia coli*: Virulence Mechanisms of a Versatile Pathogen. Elsevier Ltd, UK.

El-Hendawy, H. and Azab, E. A. (1998). Characterization and plasmid profile of inhibitory strain of *Erwinia herbicola* isolated from *Phaseolous volgaris* in Egypt. Microb. Res., 153: 341-348.

Elzahany, E. A.; Hegab, K. H.; Khalil , S. K. H. and Youssef, N. S.(2008). Synthesis, characterization and biological activity of some transition metal complexes with Schiff bases derived from 2-formylindole, salicylaldehyde, and N-amino rhodanine. Aust. J Basic Appl. Sci., 2: 210-220.

Fielding, L.; Najman, Y.; Millar, I.; Butterworth, P.; Garzanti , E.; Vezzoli, G.; Barfod ,D. and Kneller, B. (2018) The initiation and evolution of the River Nile. Earth Planet Sci Lett., 489:166‑178.

Foye, W. and Tovivich,**P.**(1977). N-glucopyranosyl-5-Aralkylidenerhodanines : Synthesis and antibacterial and antiviral activities. J. Pharm. Sci., 66: 1607-1611.

Giannella, R. A.(1996). Baron S; *et al.*, eds. *Salmonella.* In: Baron's Medical Microbiology (4th ed.). Univ. of Texas Medical Branch.

Grant, E. B.; Guiadeen , D.; Baum , E. Z.; Foleno , B. D.; Jin , H.;. Montenegro , D. A; Nelson , E. A.; Bush,K.and Hlasta,D. J.(2000).The synthesis and SAR of rhodanines as novel class C beta-lactamase inhibitors. Bioorg. Med. Chem. Lett., 10: 2179-2182.

Gualtieri, M. ; Bastide , L.; Villain-Guillot , P.; Michaux-Charachon , S.; Latouche,J.and Leonetti,**J. P.**(2006). In vitro activity of a new antibacterial rhodanine derivative against *Staphylococcus epidermidis* biofilms. J. Antimicrob. Chemother.,58: 778-783.

Hardej, D.; Ashby, Jr. C.R.; Khadtare, N.S.; Kulkarni ,S.S.; Singh, S. and Talele, T.T.(2010) The synthesis of phenylalanine-derived C5-substituted rhodanines and their activity against selected methicillin-resistant *Staphylococcus aureus* (MRSA) strains, Eur. J. Med. Chem., 45: 5827-5832.

Holmalahti, J.; Wright,A. and Raatikainen,O.(1994). Variations in the spectra of biological activities of actinomycetes isolated from different soils. Appl. Microbiol., 18: 144-146.

Klerk, C.; Fosso-Kankeu, E. ;Plessis ,L. and Waanders, F. (2017). Domestic Wastewater Treatment: The Influence of Silver Impregnated Polyrhodanine Nanofibers on Gram-Positive and Gram-Negative Bacteria.9th Int'l Conference on Advances in Science, Engineering, Technology & Waste Management (ASETWM-17) Nov. 27-28, 2017 Parys, South Africa.92-97.

Liaras, K. ; Geronikaki , A.; Glamoclija , J.;Ciric,A.and Sokovi,M.(2011).Thiazole-based chalcones as potent antimicrobial agents. Synthesis and biological evaluation, Bioorg. Med. Chem., 19: 3135-3140.

Moorthy, B.T. ; Ravi , S.; Srivastava , M.; Chiruvella, K. K.; Hamlal , H.; Joy,O. and Raghvan,S.C. (2010).Novel rhodanine derivatives induce growth inhibition followed by apoptosis, Bioorg. Med. Chem. Letts., 20: 6297-6301.

Murray, P.R.;Rosenthal,K. S.and Pfaller,**M. A.**(2009). Medical Microbiology (6th ed.). Philadelphia, PA: Mosby Elsevier.

Murugan, R.; Anbazhagan,S.and Narayanan,**S.S.** (2009). Synthesis and *in vivo* antidiabetic activity of novel dispiropyrrolidines through [3 + 2] cycloaddition reactions with thiazolidinedione and rhodanine derivatives, Eur. J. Med. Chem., 44: 3272-3279.

Navarre, W. W. and Schneewind, O.(1999). Surface proteins of gram-positive bacteria and mechanisms of their targeting to the cell wall envelope. Microbiol. Mol. Biol. Rev., 63: 174-229.

Opperman, T. J. ; Kwasny , S. M.; Williams , J. D.; Khan , A. R.; Peet , N. P.; Moir,D. T.and Bowlin ,**T. L.** (2009). Aryl rhodanines specifically inhibit staphylococcal and enterococcal biofilm formation. Antimicrob. Agents Chemother.,53:4357-4367.

Rabeh, S. A.; El-Bassat, R. A.; Tawfic,T. A. and Amer, A. S. (2007). The interaction between zooplankton and bacterial indicators of pollution in
River Nile at Cairo, Egypt African J. Biol. Sci., 3(2):91-109.

Rabeh, S. A. and Azab,E. A. (2006). Bacterial indicators of both sewage pollution and trophic status in Abu Zaabal Lakes, Egypt. Res. J. Microbiol., 1: 480-491.

Rabeh, S. A.(2010).Bacteriological Quality of Water in Rosetta Branch of the River Nile, Egypt. In: "River Deltas :Types, Structures and Ecology,Nova Science Publishers, Inc. ISBN:978-1-61728-756-5.

Sabae, S. Z. and Rabeh, S.A. (2007).Evaluation of the microbial quality of the River Nile waters at Damietta Branch, Egypt. Egyptian Journal of Aquatic Research 33(1): 301-311.

Singh, P. ;Bhavya , J.;Avadhesha,S.and Dulal P.(2012). A rhodanine derivative CCR-11 inhibits bacterial proliferation by inhibiting the assembly and GTPase activity of FtsZ .Biochemistry, 51: 5434-5442.

Song, M.X.; Deng, X.Q.; Wei, Z.Y.; Zheng, C.J.; Wu ,Y.; An, C.S.; Piao, H.R.(2015).Synthesis and Antibacterial Evaluation of (S, Z)-4-methyl-2-(4-oxo-5-((5-

substituted phenylfuran-2-yl) methylene)-2-thioxothiazolidin-3-yl) Pentanoic Acids. Iran. J. Pharm. Res. IJPR.,14(1):89-96.

Song, M.X. ; Zheng, C.J.; Deng, X.Q.; Wang , Q.; Hou, S.P.; Liu, T.T.; Xing ,X.L and Pio,H.R. (2012). Synthesis and bioactivity evaluation of rhodanine derivatives as potential anti-bacterial agents, Eur. J. Med. Chem.,54: 403-412.

Subekti, D.; Oyofo B. A. ; Tjaniadi , P.; Corwin , A. L. ; Larasati,W.; Putri,M.; Simanjuntak , C. H.; Pnjabi , N. H.; Taslim , J.; Setiawan , B.; Suree,N.; Yi , S.W.; Thieu , W.; Marohn , M.; Damoiseaux ,R .; Chan , A.; Jung , M.E. and Clubb, R.T. (2009).Discovery and structure-activity relationshipanalysis of *Staphylococcus aureus* sortase A inhibitors. Bioorganicand Medicinal Chemistry 17(20):7174-7185.

Suree, N.; Yi, S.W. and Thieu,W.(2009). Discovery and structure-activity relationship analysis of *Staphylococcus aureus sortase* A inhibitors. Bioorg Med Chem.,17:7174-785.

Tomasic, Tm.; Zidar , N.; Kovac , A.; Turk , S.; Simcic , M.; Blanot , D.; Müller-Premru , M.; Filipic , M.; Grdadolnik , S. G.; Zega, M.; Anderluh , S.; Gobec , D.; Kikelj , D. and Masic, L.P. (2009). 5- A. Benzylidenethiazolidin -4-ones as multitarget inhibitors of bacterial Mur ligases. Chem Med Chem., 5:286-295.

Toth, I. K.; Bell , K. S.; Holeva,M. C.and Birch,P. R. J.(2003). "Soft rot Erwiniae: from genes to genomes". Molecular Plant Pathology, 4: 17-30.

Won, S. J.; Liu, C.T.; Tsao, L.T.; Weng, J.R.; Ko, H.H.; Wang, J.P. and Lin, C.N. (2005).Synthetic chalcones as potential anti-inflammatory and cancer chemopreventive agents, Eur. J. Med. Chem., 40: 103-112.

Zervosen, A.; Lu , W. P.; Chen , Z.;White , R. E.; Demuth,T. P. Jr.and Frere, **J. M.** (2004).Interactions between Penicillin-Binding Proteins (PBPs) and Two Novel Classes of PBP Inhibitors, Arylalkylidene Rhodanines and Arylalkylidene Iminothiazolidin-4-ones. Antimicrob Agents Chemother., 48: 961- 969.