# Sun degradation and synthesis of new antimicrobial and antioxidant utilising poly (ethylene terephthalate) waste

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**Abstract:** Green environmentally energy source used for degradation of Poly (ethylene terephthalate), which used as versatile intermediate for the synthesis of a form of heterocyclic compounds. Triazoles 5, 6a, b, 7, 9 and 22 oxadiazol 11, thiazolidin 11, pyrazole 18 and 20 derivatives; All the structures of the newly compounds were established by the spectroscopic data such as IR, Ms and $^{1}H$ and $^{13}C$ NMR. The new heterocyclic exhibited high antimicrobial and antioxidant action.

**Keywords:** sun energy; poly (ethylene terephthalate); oxadiazole; triazole; pyrazole; thiazolidine; antimicrobial; antioxidant.

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## 1 Introduction

1,2,4-triazoles are associated with various pharmacological activities such as analgesic, antiasthmatic, diuretic, antihypertensive, anticholinergic, antibacterial, anti-fungal and anti-inflammatory activity(Fahim et al., 2017, 2018; Palekar et al., 2009; Shiradkar et al., 2007; Gürsoy and Karali, 2003; Vicini et al., 2006).It was likewise reported that many compounds containing the triazole ring possess a moderate antiviral activity (EI-Fattah et al., 1998). It was reported that the pyrazol-4-carboxylic acid hydrazides and its hydrazones possess antimicrobial activity (Ragavan et al., 2010; Fahim et al., 2017). Also 1,3,4-oxadiazoles are known to possess a wide spectrum of biological activities (Morimoto et al., 1995, Daniel and Tadeusz, 1997; Lian-Chun et al., 1997; Al-Salem et al., 2009) Nevertheless, it was reported that hydrazones possess antimicrobial activity. Recently, 1,3,4-oxadiazoles, and pyrazole have attracted special attention due to their anti-inflammatory, (Chenot, 2007; Soural et al., 2006; Kawamura et al., 2002; Krzysztof et al., 2003; Fahim et al., 2017) analgesic, ulcerogenic and lipid per-oxidation activities. Because of our interest in the synthesis of new 1,3,4-oxadiazoles, 1,2,4-triazoles, and pyrazole derivatives of biological interest (Zhuang et al., 2006; Dawood et al., 2005; Dawood and Farag, 1998; Yakout et al., 1999; Husain and Naseer, 2011) we decided to synthesise the title compounds from plastic waste for the future evaluation of their antimicrobial and antioxidant properties.

## 2 Materials and methods

Melting points were determined with an open capillary tube on an electrothermal (variable heater) melting point apparatus. Later on, the used thermometer was calibrated by using standard compounds of known mps and the melting points of the new compounds were corrected exclusively. IR spectra were recorded on a JASCO FT-IR 6,100 using KBr the bromide disc. NMR spectra were measured using JEOL E.C.A-500 MHz (1H: 500.7 MHz, 13C: 125.4 MHz) spectrometer. The mass spectra were performed at 70 eV on an MS-50 Kratos (A.E.I.) spectrometer provided with a data system. Elemental analysis of the products was carried out at the Microanalysis Laboratory, Cairo University, Cairo, Egypt, using Elemental C, H, N analyzer Vario EL II I Germany. The purity of all new samples was verified by microchemical analysis (C/H/N/S) and spectroscopy. TLC: Merck 0.2 mm silica gel 60 F254 analytic aluminum plates. All international principles and local regulations concerning the care and use of laboratory animals were considered during the pharmacological screening.

### *2.1 General procedure*

Plastic bottles (22 g) were cut into small strips, mixed with NaOH (12 g) and placed in sun light for five weeks to obtain the sodium salt of terepthalate. The resulting materials were dissolved in water, followed by acidification using $H_2SO_4$ (5 mol/L) to afford a white precipitate of terephthalic acid (*1*), yield 90%; m.p. above 300°C. *Terephthalic acid* (Fahim et al., 2013, 2014, 2016) (10 g, 1.66 mol) was refluxed in absolute butanol (30 ml) and $H_2SO_4$ (5ml) for 6 h to give a mixture of *Dibutylterephthalate* (*2a*) and *4-*(*butoxycarbonyl*) *benzoic acid* (*2b*).

*Dibutylterephthalate* (*2a*) was obtained as yellow oil from the mixture was concentrated under reduced pressure and crude product was purified by silica gel chromatography eluting with petroleum ether/ ethylacetate (95:5), 80% yield. IR (KBr) $\nu_{max}/cm^{-1}$: 1,723 (C=O); $^1H$ NMR (DMSO-$d_6$): 0.853 (t, 6H), 1.003 (m, 4H), 1.87 (m, 4H), 4.19 (t, 4H), 8.10 (s, 4H,); m/z (%) 278 ($M^+$, 100.0%), 216 (27.5%); anal calcd for $C_{16}H_{22}O_4$ (278.15): C, 69.04%; H, 7.97%; found C, 69.00%; H, 7.90%.

While *4-(butoxycarbonyl) benzoic acid* (*2b*) were separated by washing with 10% $Na_2CO_3$ and recrystallised from EtOH as white solid in 20% yield; m.p 116°C; IR(KBr) $\nu_{max}/cm^{-1}$: 3,066 (OH), 1,722, 1,693 (C=O), 2,961, 2,872 (CH); $^1H$ NMR (DMSO-$d_6$): 0.89 (t, 3H), 1.3 (m, 2H), 1.6 (m, 2H), 4.02 (s, 1H, *H*O, $D_2O$ exchangeable ), 4.13 (t, 2H), 7.95 (dd, J = 12 Hz, 2H), 8.01 (dd, *J* = 12 Hz, 2H); m/z (%) 206 ($M^+$, 100.0%), 191 (27.5%); anal calcd for $C_{12}H_{14}O_4$ (222.09): C, 64.85%; H, 6.35%; found C, 64.80%; H, 6.83%.

#### *2.1.1 Reactions of 4-butyrylbenzohydrazide (3)*

Dibutyl-terepthalate (*2a*) (10 ml) in hydrazine hydrate (1.4 ml) was refluxed in absolute ethanol (30ml) for 8 h to white solid which filtered off and washed with ether, dried and finally recrystallised from ethanol to afforded *4-butyrylbenzohydrazide* (*3*), 87% yield; m.p 300°C; IR(KBr) $\nu_{max}/cm^{-1}$: 3,321 (NH), 1,659 (C=O), 1,612 (C=O), $cm^{-1}$; $^1H$ NMR (DMSO-$d_6$): 1.009 (t, 3H), 1.379 (m, 2H), 1.660 (m, 2H), 3.73 (t, 2H), 4.24 (dd, 2H, $H_2N$, $D_2O$ exchangeable ), 7.81(dd, 2H), 7.96 (dd, 2H), 9.83 (t, 1H, HN, $D_2O$ exchangeable);

$^{13}$C NMR (DMSO-$d_6$ ):δ: 13.8, 18.9, 31.1, 64.5, 93.5, 114.1, 115.8, 119.8, 125.9, 130.9, 135.5, 142.6, 163, 167.9, m/z(%) 236 ($M^+$, 100.0%), 191 (27.5%); anal calcd $C_{12}H_{16}N_2O_3$ (236.27) C, 61.00%; H, 6.83%, N, 11.86%; found C, 61.23%; H, 6.88%, N, 11.80%.

### *2.1.2 Synthesis of potassium thiocarbazinate (4)*

Ethanolic potassium hydroxide solution (25 ml) was cooled in ice bath with 4-butyrylbenzohydrazide (*3*) (1 mmole) was added with stirring. To this carbon disulfide (5 mmole) was added in small portion wise with constant stirring. The reaction mixture was agitated continuously for 12 h at room temperature. The precipitated potassium thiocarbazinate *4* was collected by filtration, washed with cold ethanol (50 ml) and dried in vacuum. The potassium salt thus obtained was used in next step without further purification.

Suspension of potassium thiocarbazinate *4* (1 mmole) in water (5 ml) and hydrazine hydrate (99%, 3 mmole) was heated for 18 h at 100°C with occasional shaking. The colour of the reaction was changed to green with evolution of hydrogen sulphide gas. A homogenous reaction mixture was obtained during reaction process. The reaction mixture was cooled to room temperature and diluted with cold water (20 ml). On acidification with HCl the required triazole was precipitated out, which was recrystallised with DMF/$H_2O$ (1:2) to obtain *4*-(*5-mercapto-4-amino-1,3,4-triazole*) *benzoic acid* (*5*), 80% yield, mp: 235°C; IR (KBr) $\nu_{max}/cm^{-1}$: 3,855 (OH), 3,434 ($NH_2$), 1,623 (C=O); $^1$H NMR (DMSO-$d_6$): 4.2 (s, 2H,), 7.99 (s, 2H,), 8.11 (s, 2H), 11.2 (s, 1H, *H*O $D_2O$ exchangeable), 14.03 (s, 1H, *H*S $D_2O$ exchangeable); $^{13}$C NMR (DMSO-$d_6$): δ: 127, 128, 128.4, 129.7, 142, 155, 167; m/z (%) 236 ($M^+$, 100.0%), 180 (41.49%); anal calcd $C_9H_8N_4O_2S$ (236.25) C, 45.75%; H, 3.41%, N, 23.72%, S, 13.57%; found C, 45.77%; H, 3.42%, N, 23.65%, S,13.59%.

### *2.1.3 Synthesis of (E)-4-(5-mercapto) 4H-1,2,4-triazol-3-yl) benzoic acid derivatives (6a,b)*

A solution of five (10 mmol) in glacial acetic acid (10 ml) was allowed to react with the appropriate aldehydes (10 mmol) under reflux for 2 h. The reaction mixture was then cooled and the precipated arylidines derivatives was filtered off, washed with water, dried and recrystallised from appropriate solvent to afford the title compounds.

(*E*)-*4*-(*4*-(*4-fluorobenzylideneamino*)-*5-mercapto-4H-1,2,4-triazol-3-yl*) *benzoic acid* (*6a*): yield 66% mp: 275°C; IR (KBr) $\nu_{max}/cm^{-1}$: 3,230 (OH), 3,121 (NH), 1,665 (C=O); $^1$HNMR (DMSO-$d_6$): δ: 7.22 (d, 2H), 7.38 (d, 2H), 8.03–8.3 (m, 4H), 10.2 (s, 1H); 10.9 (s, 1H, *H*O $D_2O$ exchangeable), 13.51 (s, 1H, *H*S $D_2O$ exchangeable); $^{13}$C NMR (DMSO-$d_6$): δ: 115, 127, 130, 135, 151.1, 154, 159, 165.2, 169, m/z (%) 342 ($M^+$, 100.0%); analysis for $C_{16}H_{11}FN_4O_2S$ (342.35); C, 56.13; H, 3.24; N, 16.37; S, 9.37; F, 5.55%; found: C, 56.10; H, 3.20; N, 16.42; S, 9.39; F, 5.60%.

(*E*)-*4*-(*5-mercapto-4*-(*4-methoxybenzylideneamino*)-*4H-1,2,4-triazol-3-yl*) *benzoic acid* (*6b*): yield 72% mp: 280°C; IR (KBr) $\nu_{max}/cm^{-1}$: 3,251 (OH), 3,121 (NH), 1,652 (C=O); $^1$HNMR (DMSO-$d_6$): δ: 3.8(s, 3H), 7.08 (d, 2H), 7.5 (d, 2H); 7.8 (m, 4H), 9.87 (s, 1H), 10.9 (s, 1H, *H*O $D_2O$ exchangeable), 13.08 (s, 1H, *H*S $D_2O$ exchangeable); m/z: 354 ($M^+$, 100.0%); anal calcd $C_{17}H_{14}N_4O_3S$ (354.38); C, 57.62; H, 3.98; N, 15.81; S, 9.05; % found: C, 57.58; H, 4.01; N, 15.80; S, 9.03%.

### *2.1.4 Reactions of compound 5 with 2-aminobenzenethiol*

Mixture of *5* (1 mmol) with 2-aminobenzenethiol (1 mmol) in $POCl_3$ for 3 h. The reaction mixture was cooled to room temperature and then gradually poured on to crushed ice with stirring. The mixture was neutralised with $NaHCO_3$ solution and allowed to stand overnight then crystallised EtOH /DMF.

*4-amino-5-*(*4-*(*benzo*[*d*]*thiazol-2-yl*) *phenyl*)*-4H-1,2,4-triazole-3-thiol* (*7*) Yield 65% mp: 250°C; IR (KBr) $\nu_{max}/cm^{-1}$: $^1$3,873 ($NH_2$), 1637 (C=O); $^1$HNMR (DMSO-$d_6$): δ: 5.3 (s, 2H, $H_2ND_2O$ exchangeable), 6.7 (d, 2H), 7.16 (d, 4H), 7.18 (d, 2H), 7.3(d, 1H), 13.7 (s,1H, *H*S $D_2O$ exchangeable); $^{13}$C NMR (DMSO-$d_6$): δ: 121 125, 128, 133, 143, 151, 154, 167, 169.3; m/z: 325($M^+$, 100.0%), 244 (70%); anal calcd $C_{15}H_{11}N_5S_2$ (325.05); C,55.36; H, 3.41; N, 21.52; S, 19.71; % found: C, 55.25; H, 3.45; N, 21.49; S, 19.65%.

### *2.1.5 Reaction of compound 7 with methyl idodide*

Compound *7* (1 mmol) with methyl idodide (1 mmol) in solution of KOH/EtOH in ice bath for 24 h then filtered and get the precipitation *4-*(*4-amino-5-*(*methylthio*)*-4H-1,2, 4-triazol-3-yl*) *benzoic acid* (*10*) yield 75% mp: 241°C; IR (KBr) $\nu_{max}/cm^{-1}$: 3,750 (OH), 3,315 ($NH_2$), 1,623 (C=O); $^1$HNMR (DMSO-$d_6$): δ: 2.53 (s, 3H), 5.2 (s, 2H), 7.99–8.1 (m, 4H), 10.2 (s, 1H, *H*O $D_2O$ exchangeable), m/z: 250($M^+$, 100.0%); anal calcd $C_{10}H_{10}N_4O_2S$ (250.28);C, 47.99; H, 4.03; N, 22.39; S, 12.81; %, found: C, 47.98; H, 4.05; N, 22.40; S, 12.80%.

Reaction of triazole *8* with ethylbromoacetate in EtOH for 5 h. The reaction mixture was then cooled and the predicated was filtered off, washed with water, dried and recrystallised from EtOH/DMF to afford *4-*(*4-amino-5-*(*2-ethoxy-2-oxoethylthio*)*-4H-1,2,4-triazol-3-yl*) *benzoic acid* (*9*) yield 71% mp:255°C; IR (KBr) $\nu_{max}/cm^{-1}$: $^1$3,426 ($NH_2$), 1,741 (C=O), 1,632 (C=O); $^1$HNMR (DMSO-$d_6$): δ:1.29 (t, 3H), 3.3 (q, 2H), 3.6 (s, 2H, $H_2N$ $D_2O$ exchangeable), 5.2 (s, 2H), 7.6 (d, 2H),7.7 (d, 2H), 9.2 (s, 1H, *H*O $D_2O$ exchangeable); m/z: 322($M^+$, 100.0%); anal calcd $C_{13}H_{14}N_4O_4S$ (322.34); C, 48.44; H, 4.38; N, 17.38; S, 9.95; %, found: C, 48.50; H, 4.40; N, 17.22; S, 9.90%.

### *2.1.6 Synthesis of butyl 4-(aminocarbamoyl) benzoate derivatives 10a,b*

An equimolar quantity of *3* (1 mmole) and different aromatic aldehydes (1 mmol) was refluxed in alcohol for 4 h in presence of few drops of glacial acetic acid. The reaction mixture on cooling was poured into cold water, filtered and dried. The crude solid was recrystallised in DMF/$H_2O$ mixture to give the products.

*Butyl 4-*(*4-fluorobenzylideneaminocarbamoyl*) *benzoate* (*10a*); yield 70% mp:236°C (yellow solid); IR (KBr) $\nu_{max}/cm^{-1}$: 3,262 (NH), 1,719 (C=O), 1,648 (C=O); $^1$HNMR (DMSO-$d_6$): δ:0.91 (t, 3H), 1.40 (m, 2H), 1.68 (m, 2H), 4.28 (t, 2H), 7.28 (d, 2H), 7.78 (d, 2H), 8.00 (d, 2H), 8.19 (d, 2H), 8.6 (s, 1H), 11.99 (s, 1H, *H*N, $D_2O$ exchangeable) ; m/z: 149 ($M^+$, 100.0%), 166(62.23%); anal calcd $C_{19}H_{19}FN_2O_3$ (342.36); C, 66.66; H, 5.59; N, 8.18; F, 5.55%; found: C, 66.65; H, 5.60; N, 8.19; F, 5.56%.

*Butyl 4-*(*4-bromobenzylideneaminocarbamoyl*)*benzoate* (*10b*); yield 69% mp:233°C (yellow); IR (KBr) $\nu_{max}/cm^{-1}$: $^1$3,267 (NH), 1,719 (C=O), 1,648 (C=O); $^1$HNMR (DMSO-$d_6$): δ:0.91(t, 3H), 1.40 (m, 2H), 1.68 ( m, 2H), 4.28 (t, 2H), 7.28 (d, 2H), 7.78 (d, 2H), 8.00 (d, 2H), 8.19 (d, 2H), 8.6 (s, 1H), 11.99 (s, 1H, *H*N, $D_2O$ exchangeable); $^{13}$C NMR (DMSO-$d_6$): δ 13.8, 18.9, 31.1, 64, 125, 127, 129, 131.7, 133, 163, 166; m/z: 211

($M^+$, 100.0%), 238 (62.23%); anal calcd $C_{19}H_{19}BrN_2O_3$ (404.06); C, 56.59; H, 4.75; N, 6.95; Br, 19.81%; found: C, 56.60; H, 4.77; N, 6.96; Br, 19.82%.

### *2.1.7 Synthesis of 1-(4-(4-acetyl-5-(4-fluorophenyl)-4,5-dihydro-1,3, 4-oxadiazol-2-yl)phenyl) pentan-1-one (11)*

Compound *10a* (1 mmol) was refluxed in glacial acetic acid (25 ml) for eight hours; the reaction mixture was then partially concentrated and cooled. The precipitated formed was filtered off and crystallised from AcOH.

*1-*(*4-*(*4-acetyl-5-*(*4-fluorophenyl*(*-4,5-dihydro-1,3,4-oxadiazol-2-yl*)*phenyl*)*pentan-1-one* (*11*);yield 82% mp: 260°C (orange); IR (KBr) $v_{max}/cm^{-1}$: 1,694 (C=O), 1,643 (C=O); $^1$HNMR (DMSO-$d_6$): δ:0.92 (t, 3H), 1.40 (m, 2H), 1.68( m, 2H), 2.53 (s, 3H), 4.29 (t, 2H), 6.61 (s, 1H), 6.9 (d, 2H), 7.8 (d, 2H), 8.00 (d, 2H), 8.05 (d, 2H); m/z: 384 ($M^+$, 100.0%), 256 (12.23%); anal calcd $C_{21}H_{21}FN_2O_4$ (384.40); C, 65.62; H, 5.51; N, 7.29; F, 4.49%; found: C, 65.66; H, 5.50; N, 7.30; F, 4.95%.

### *2.1.8 Synthesis of Butyl 4-(2-(4-bromophenyl)-4-oxothiazolidin-3-ylcarbamoyl)benzoate (12b)*

A mixture of hydrazones *10b* (1 mmol) and thioglycolic acid (1 mmol) was refluxed in dry benzene (*25* ml) for 8–10 h. After completion of reaction excess benzene was evaporated in vacuo. The resulting residue was neutralised with saturated $NaHCO_3$ solution until $CO_2$ evolution ceased. The solid product was washed with water, dried and recrystallised from DMF/$H_2O$.

*Butyl 4-*(*2-*(*4-bromophenyl*)*-4-oxothiazolidin-3-ylcarbamoyl*)*benzoate* (*12b*) yield 77% mp: 240°C (white); IR (KBr) $v_{max}/cm^{-1}$: 3,433 (NH), 1,719 (C=O), 1,650 (C=O); $^1$HNMR (DMSO-$d_6$): 0.91 (t, 3H), 1.40 (m, 2H), 1.68 ( m, 2H), 3.38 (dd, 2H, ($J$ = 8.02)), 4.29 (t, 2H), 5.29 (s, 1H,), 6.95 (d, 2H), 7.31 (d, 2H), 8.03 (d, 4H), 11.99 (s, 1H, *H*N, $D_2O$ exchangeable); $^{13}$C NMR (DMSO $d_6$ ):13.8, 19.1, 31.2, 35.7, 57.3, 64.6, 121, 127, 130, 131, 133.6, 138, 164.9, 166; m/z: 222 ($M^+$, 100.0%), 476 (0.3%); anal calcd $C_{21}H_{21}BrN_2O_4S$ (476.04) C, 52.48; H, 4.43; N, 5.87; S, 6.72; Br, 16.74%; found: C, 52.86; H, 4.49; N, 5.77; S, 6.73; Br, 16.50%.

### *2.1.9 Synthesis of 4-(2-cyanoacetyl) benzoic acid (13)*

Reaction of 4-pentanoylbenzoic acid (*2b*) (10 mmole) with $CH_3CN$ (10 mmole) in dry THF and stirring well to dissolve completely then add equivalent weight of NaH and DMF then refluxed to 100°C for 2 h until effervesce and then be cool and washed it by petroleum ether and get salt then be dissolve in ice water and acidified by 0.5 M of HCl to get the corresponding *4-*(*2-cyanoacetyl*) *benzoic acid* (*13*); yield white in 75%; mp 170°C–172°C; IR (KBr) $v_{max}/cm^{-1}$: 3,374 (OH), 2,237 (CN), 1,689 (C=O), 1,602 (C=O); $^1$HNMR (DMSO-$d_6$): 3.67 (s, 1H, *H*O $D_2O$ exchangeable), 4.4 (s, 2H), 8.09 (d, 2H), 8.1 (d, 2H); $^{13}$C NMR (DMSO-$d_6$): δ 29.77, 129, 130, 134, 135, 165, 170; m/z: 149 ($M^+$, 100%), 179 (83.8%), 120 (70.4%); anal calcd $C_{10}H_7NO_3$ (189.17); C, 63.49; H, 3.73; N, 7.40; %; found: C, 63.50; H, 3.77; N, 7.44;%.

### *2.1.10 Synthesis of butyl 4-(benzo[d]thiazol-2-yl)benzoate (14)*

To a mixture of 4-pentanoylbenzoic acid (*2b*) (1.5 g, 10 mmol) and 2-aminobenzenethiol (10 mmol) was mixed in $POCl_3$ was refluxed for 2 h. The reaction mixture was poured on ice and be neutralised by $Na_2CO_3$ get of green solid, dried and finally recrystallised from ethanol/DMF to *butyl 4-*(*benzo*[*d*]*thiazol-2-yl*)*benzoate* (*14*),yield 90%; m.p. 200°C,IR (KBr) $v_{max}/cm^{-1}$: 1,722 (C=O), 2,960 (CH aliphatic);$^1$H NMR (DMSO-$d_6$): δ 0.9 (t, 3H), 1.46 (m, 2H), 1.73 (m, 2H), 4.31 (t, 2H), 7.4 (d, 2H), 7.8 (d, 2H), 8.06–8.07 (d, 2H), 8.12–8.13 (d, 2H), m/z: 55 ($M^+$, 100.0%), 210 (26.87%), anal calcd $C_{18}H_{17}NO_2S$ (311.40): calcd: C, 69.43; H, 5.50; N, 4.50% found: C, 69.45; H, 5.53;N, 4.52%.

Compound *14* (10 mmole) reacts with $CH_3CN$ (10 mmole) in dry THF and stirring well to dissolve completely then add equivalent weight of NaH and DMF then refluxed to 100°C for 2 h until effervesce and then be cool and washed it by petroleum ether and get salt then be dissolve in ice water and acidified by 0.5 M of HCl to get the corresponding *3-*(*4-*(*benzo*[*d*]*thiazol-2-yl*)*phenyl*)*-3-oxopropanenitrile* (*15*), and be crystallised into the acetic acid, yield 81%; m.p. 225°C. IR(KBr) $v_{max}/cm^{-1}$: 3,428 (OH), 2,543 (CN), 1,688 (C=O); $^1$H NMR (DMSO-$d_6$): δ 3.8 (s, 2H), 6.4–6.5 (t, 2H), 6.7–6.8 (d, 2H), 6.7–6.8 (d, 2H), 7.05–7.11 (d, 2H), 8.06–8.07 (d, 2H), 8.12–8.13 (d, 2H) m/z: 278 ($M^+$, 100.0%), 282 (37.5%), anal calcd $C_{16}H_{10}N_2OS$ (278.33): calcd: C, 69.04; H, 3.62; N, 10.06% found: C, 69.10; H, 3.65; N, 10.09%.

### *2.1.11 Coupling of 3-oxo-3-phenylpropanenitrile derivatives 13, 15 with aromatic diazonium salts*

To a cold solution of 3-oxo-3-phenylpropanenitrile derivatives *13* and *15* (0.44 g 4 mmol) in ethanol (50 ml), and sodium acetate trihydrate (3 g), was added the appropriate diazonium salt of the corresponding aromatic amines. The addition was carried out portionwise with stirring at 0–5°C over a period of 30 minutes. After complete addition, the reaction mixture was stirred for further 4 h then kept in an ice chest for 12 h and finally diluted with water. The precipitated solid was collected by filtration, washed with water, dried and finally recrystallised from the appropriate solvent to afford the corresponding hydrazones *16*. The physical and spectral data of are listed below:

- *4-*(*2-*(*2-*(*4-bromophenyl*)*hydrazono*)*-2-cyanoacetyl*) *benzoic acid* (*16a*), Yield 77% mp: 211°C (white), IR (KBr) $v_{max}/cm^{-1}$: 3,433 (OH), 3,233 (NH), 2,210 (CN), 1,689 (C=O), 1,630 (C=O);$^1$HNMR (DMSO-$d_6$): δ 4.1(dd, 1H, *H*N, $D_2O$ exchangeable), 7.2 (dd, 2H), 7.5 (dd, 2H), 7.6–8.1(m, 4H), 12.5 (s, 1H, *H*O $D_2O$ exchangeable); m/z: 91 ($M^+$, 100.0%), 155 (93.56%); anal calcd $C_{16}H_{10}BrN_3O_3$(372.17) calcd: C, 51.63; H, 2.71; N, 11.29; Br, 21.47; found: C, 51.63; H, 2.70; N, 11.30; Br, 21.48.
- *4-*(*2-*(*2-*(*4-carboxyphenyl*)*-1-cyano-2-oxoethylidene*)*hydrazinyl*) *benzene sulfinate* (*16b*), Yield 75% mp:230°C (white), IR (KBr) $v_{max}/cm^{-1}$: 3,423 (OH), 3,216 (NH), 2,222 (CN), 1,704 (C=O), 1,649(C=O); $^1$HNMR (DMSO-$d_6$): δ 4.5(dd, 1H, *H*N, $D_2O$ exchangeable), 7.2 (dd, 2H), 7.5 (dd, 2H), 7.6–8.1 (m,4H), 12.5 (s, 1H, *H*O $D_2O$ exchangeable); m/z: 245 ($M^+$, 100.0%), 149 (84.8%), 77 (94.56%); anal calcd $C_{16}H_{10}N_3O_5S$ (356.33), calcd: C, 53.93; H, 2.83; N, 11.79; S, 9.00% found: C, 53.99; H, 2.80; N, 11.72; S, 8.99.

- *4-(2-cyano-2-(2-(4-fluorophenyl)hydrazono)acetyl) benzoic acid* (*16c*) Yield 66% mp: 245°C, IR (KBr) $\nu_{max}/cm^{-1}$: 3,423 (OH), 3,216 (NH), 2,222 (CN), 1,704 (C=O), 1,649 (C=O);$^1$HNMR (DMSO-$d_6$): δ 4.5 (dd, 1H, *H*N, $D_2O$ exchangeable), 7.2 (dd, 2H), 7.5 (dd, 2H), 7.6–8.1 (m, 4H), 12.5 (s, 1H, *H*O $D_2O$ exchangeable); m/z: 311 ($M^+$, 100.0%); anal calcd $C_{16}H_{10}FN_3O_5S$ (311.07), calcd: C, 61.74; H, 3.24; N, 13.50; F, 6.10 found: C, 61.77; H, 3.28; N, 13.52; F, 6.12.

- (*E*)-*4-(2-cyano-2-(2-phenylhydrazono)acetyl)benzoic acid* (*16d*), yield 66% mp: 216°C, IR (KBr) $\nu_{max}/cm^{-1}$: 3,454 (OH), 3,193 (NH),1,937 (CN), 1,714 (C=O), 1,599 (C=O); $^1$HNMR (DMSO-$d_6$): δ 4.5 (dd, 1H, *H*N $D_2O$ exchangeable), 6.81 (dd, 1H), 7.20–7.35 (m, 4H), 7.6–8.1(m, 4H), 12.5 (s,1H, *H*O $D_2O$ exchangeable); m/z: 293 ($M^+$, 100.0%); anal calcd $C_{16}H_{11}N_3O_5S$ (293.28) calcd: C, 65.53; H, 3.78; N, 14.33; found: C, 65.50; H, 3.79; N, 14.34.

- *2-(4-(benzo[d]thiazol-2-yl)phenyl)-N'-(4-bromophenyl)-2-oxoacetohydrazonoylcyanide* (*16e*), Yield 65% mp:266°C, IR (KBr) $\nu_{max}/cm^{-1}$: 33 (NH), 2,545 (CN), 1,688 (C=O); $^1$HNMR (DMSO-$d_6$):, δ 7.9–8 (m, 4H), 8.07 (dd, 2H (*J* = 1.03), 8.15 (dd, 2H (*J* = 1.03)), 8.3 (m, 4H,), 10.6 (s, 1H, *H*N $D_2O$ exchangeable); m/z: 461 ($M^+$, 100.0%), 462 (60%); anal calcd $C_{22}H_{13}BrN_4OS$ (461.33) calcd: C, 57.28; H, 2.84; N, 12.14; S, 6.95; Br, 17.32; found: C, 57.30; H, 2.83; N, 12.15; S, 6.94; Br, 17.30.

- *2-(4-(benzo[d]thiazol-2-yl)phenyl)-N'-(4-fluorophenyl)-2-oxoacetohydrazonoylcyanide* (*16f*), Yield 71% mp:240°C (white)IR (KBr) $\nu_{max}/cm^{-1}$: 3,432 (NH), 2,545 (CN), 1,688 (C=O); $^1$HNMR (DMSO-$d_6$):, 7.47–7.48 (m,4H), 7.53 (dd, 2H, (*J* = 12.03)), 7.55 (dd, 2H, (*J* = 12.03)), 8–8.09 (m, 4H), 10.35 (s, 1H, *H*N $D_2O$ exchangeable); m/z: 63($M^+$, 100.0%), 403 (59.1%), 163 (77.3%), 211 (81.8%) ; anal calcd $C_{22}H_{13}FN_4OS$ (400.43) calcd: C, 65.99; H, 3.27; N, 13.99; S, 8.01; F, 4.74; found: C, 65.98; H, 3.28; N, 14.00; S, 8.03; F, 4.75%.

### *2.1.12 Reactions of of 3-oxo-3-phenylpropanenitrile derivatives 13 and 15 with phenyl isothiocyanate*

To a solution of compound *13* and *15* (0. 4 g, 2 mmol) in absolute ethanol (20 mL) containing triethylamine (five drops), elemental sulfur (0.06 g, 2 mmol) and phenylisothiocyanate (0.27 g, 2 mmol) were added. The reaction mixture was heated at 60°C for 2 h with continuous stirring and then poured onto beaker containing an ice/water mixture containing few drops of hydrochloric acid. The formed solid product was collected by filtration, dried well, and recrystallised from DMF/ethanol mixture (3:1) to give 17 respectively.

*4-(4-amino-3-phenyl-2-thioxo-2,3-dihydrothiazole-5-carbonyl) benzoic acid* (*17a*), Yield 66% mp: 259°C, IR (KBr) $\nu_{max}/cm^{-1}$: 3,428 (OH), 3,065 ($NH_2$), 1,684 (C=O), 1,572 (C=O); $^1$HNMR (DMSO-$d_6$): δ 6.7 (d, 2H), 7.3 (t, 1H), 7.4 (d, 2H), 7.9–8.0(m, 4H), 8.5 (s, 2H, $H_2N$ $D_2O$ exchangeable), 12.0 (s, 1H, *H*O $D_2O$ exchangeable); m/z: 356 ($M^+$, 100.0%); anal calcd; $C_{17}H_{12}N_2O_3S_2$ (356.42) calcd: C, 57.29; H, 3.39; N, 7.86; S, 17.99; found: C, 57.30; H, 3.40; N, 7.88; S, 18.00.

(*4-amino-3-phenyl-2-thioxo-2,3-dihydrothiazol-5-yl*) (*4-(benzo[d]thiazol-2-yl)phenyl*) *methanone* (*17b*),Yield 62% mp: 245°C, IR (KBr) $\nu_{max}/cm^{-1}$: 3,340 ($NH_2$), 1,600 (C=O); $^1$HNMR (DMSO-d*6*): δ 4.0(s, 2H) 4.9 (s, H, *H*S $D_2O$ exchangeable), 7.0–7.2 (m, 5H),

7.4–7.47(m, 4H), 7.6–8.27 (m, 4H), 11.06 (s, 1H, $H_2$N $D_2O$ exchangeable); m/z: 447 ($M^+$, 100.0%); anal calcd; $C_{23}H_{17}N_3OS_3$ (447.60), calcd: C, 61.72; H, 3.83; N, 9.39; S, 21.49; found: C, 61.70; H, 3.88; N, 9.40; S, 21.44.

### *2.1.13 Reactions of of 3-oxo-3-phenylpropanenitrile derivatives 13 and 15 with ethyl 2-(2-(4-methoxyphenyl) hydrazono)-2-chloroacetate*

3-Oxo-3-phenylpropanenitrile derivatives *13* and *15* (1 mmol) was added to an ethanolic sodium ethoxide solution prepared from sodium metal (1 mmol) and absolute ethanol (15 ml) with stirring. After stirring for 20 min, the appropriate hydrazonoyl halide (1 mmol) was added portion wise to the resulting solution and the reaction mixture was stirred for further 12 h at room temperature. The formed solid was filtered off, washed with water and dried. Recrystallisation from the proper solvent afforded the amino-pyrazole derivative *18*. The physical and spectral data of the amino-pyrazole are listed below:

- *4-*(*5-amino-3-*(*ethoxycarbonyl*)*-1-*(*p-tolyl*)*-1H-pyrazole-4-carbonyl*) *benzoic acid* (*18a*):Yield 45% mp: 214°C, IR (KBr) $\nu_{max}/cm^{-1}$: 3,346 (OH), 3,219 ($NH_2$), 1,716 (C=O), 1,642 (C=O), 1,602 (C=O); $^1$HNMR (DMSO-$d_6$): δ 1.29 (t, 3H), 2.5 (s,3H), 3.36 (q, 2H), 7.21–7.24 (m,4H), 7.35 (s, 2H, $H_2$N, $D_2O$ exchangeable), 7.37–7.4 (m, 4H), 12.5 (s, 1H, *H*O $D_2O$ exchangeable); m/z: 149 ($M^+$, 100.0%), 393 (3.46%), 166 (65.44%); anal calcd $C_{21}H_{19}N_3O_5$ (393.39) calcd: C, 64.12; H, 4.87; N, 10.68; found: C, 58.91; H, 3.43; N, 14.72.
- *Ethyl-5-amino-4-*(*4-*(*benzo*[*d*]*thiazol-2-yl*)*benzoyl*)*-1-*(*4-chlorophenyl*)*-1H-pyrazole-3-carboxylate* (*18b*), yield 50% mp: 253°C IR (KBr) $\nu_{max}/cm^{-1}$: 3,422 ($NH_2$), 1,688 (C=O), 1,606 (C=O); $^1$HNMR (DMSO-$d_6$): δ 1.1–1.3 (t, 3H), 4.3 (q, 2H), 7.4–7.5 (m, 4H), 7.99 (s, 2H, $H_2$N, $D_2O$ exchangeable), 8.05–8.15 (m, 4H), m/z: 77 ($M^+$, 100.0%), 403 (20%), 503 (32.5%); anal calcd $C_{26}H_{19}ClN_4O_3S$ (502.97), calcd: C, 62.09; H, 3.81; N, 11.14; S, 6.38; Cl, 7.05; found: C, 62.10; H, 3.83; N, 11.15; S, 6.34 Cl, 7.03%.

### *2.1.14 Reaction of hydrazone 16a–c with chloro acetonitrile*

To the corresponding hydrazone *16a–c* (4 mmol) in ethanol (10 ml), in the presence of catalytic amount of triethylamine was added with chloroacetonitrile (1 mmol) and the mixture was refluxed for 4 h. The formed precipitate was filtered off, washed with ethanol and dried. Recrystallisation from ethanol afforded the corresponding aminopyrazole derivatives *20a–c*.

*4-*(*4-amino-1-*(*4-bromophenyl*)*-5-cyano-1H-pyrazole-3-carbonyl*)*benzoic acid* (*20a*) Yield 70% mp: 255°C; IR (KBr) $\nu_{max}/cm^{-1}$: 3,743 (OH), 3,261 (NH), 2,456 (CN), 1,712 (C=O), 1,560 (C=O); $^1$HNMR (DMSO-$d_6$): 4.32 (s, 2H, $H_2$N $D_2O$ exchangeable), 7.0–7.2 (m, 4H), 7.4–8.04 (m, 4H), 12.5 (s, 1H, *H*O $D_2O$ exchangeable); $^{13}$C NMR (DMSO $d_6$):113, 115, 118, 129, 130, 136, 142, 158, 169, 198; m/z: 411($M^+$, 100.0%), 367 (73.37%); anal calcd $C_{18}H_{11}BrN_4O_3$ (411.21) C, 52.57; H, 2.70; N, 13.62; Br 19.43%; found: C, 52.55; H, 2.70; N, 13.64; Br 19.44%.

*4-*(*4-amino-3-*(*4-carboxybenzoyl*)*-5-cyano-1H-pyrazol-1-yl*)*benzenesulfinate* (*20b*) Yield 66% mp: 240°C; IR (KBr) $\nu_{max}/cm^{-1}$: 3,743 (OH), 3,261 (NH), 2,456 (CN), 1,712 (C=O), 1,560 (C=O); $^1$HNMR (DMSO-$d_6$): 4.32 (s, 2H, $H_2$N, $D_2O$ exchangeable),

7.0–7.2 (m, 4H), 7.4–8.04 (m, 4H), 12.5 (s, 1H, *H*O D*2*O exchangeable); m/z: 395 ($M^+$, 100.0%); anal calcd $C_{18}H_{11}N_4O_5S$ (395.37) C, 54.68; H, 2.80; N, 14.17; S 8.11%; found: C, 54.66; H, 2.83; N, 14.18; S 8.11%.

*4-(4-amino-5-cyano-1-phenyl-1H-pyrazole-3-carbonyl)benzoic acid (20c*) Yield 52% mp: 245°C; IR (KBr) $\nu_{max}/cm^{-1}$: 3,454 (OH), 3,193 (NH), 1,937 (CN), 1,714 (C=O), 1,599 (C=O); $^1$HNMR (DMSO-$d_6$): 4.32 (s, 2H, $H_2$N, $D_2O$ exchangeable), 7.0–7.2 (m, 4H), 7.4–8.04 (m, 4H,), 12.5 (s, 1H, *H*O $D_2O$ exchangeable); m/z: 332($M^+$, 100.0%); anal calcd $C_{18}H_{12}$ $N_4O_3$ (332.31) C, 65.06; H, 3.64; N, 16.86; %; found: C, 65.05; H, 3.62; N, 16.88%.

### *2.1.15 Reaction of hydrazone (16a–c) with hydroxylamine hydrochloride*

1-Hydroxylamine hydrochloride (0.1 mol) was added to a solution of hydrazono)-2-cyanoacetyl)benzoic acid derivative 16a-c (0.1 mol) in (50 mL) ethanol, then 0.1 mol of anhydrous sodium acetate was added and the reaction mixture was refluxed for 1 h and then left to cool to room temperature. The solid product so-formed was filtered and crystallised from ethanol.

- *4-((2E)-3-amino-2-(2-(4-bromophenyl)hydrazono)-3-(hydroxyimino)propanoyl) benzoic acid* (*21a*); yield 66% mp:275°C; IR (KBr) $\nu_{max}/cm^{-1}$: 3,415 (OH), 3,221 (OH), 3,004 ($NH_2$), 1,697 (C=O), 1,653 (C=O); $^1$HNMR (DMSO-$d_6$): 2.5 (s, 1H, *H*O $D_2O$ exchangeable), 6.25–7.3(m, 4H),7.5 (s, 1H, *H*N, $D_2O$ exchangeable), 8.0–8.1 (m, 4H,), 8.5 (1H, $H_2ND_2O$ exchangeable), 11.8 (s, 1H, *H*O $D_2O$ exchangeable); m/z: 405($M^+$, 100.0%); anal calcd $C_{16}H_{13}Br$ $N_4O_4$ (405.20) C, 47.43; H, 3.23; N, 13.83; Br 19.72%; found: C, 47.40; H, 3.25; N, 13.85; Br 19.77%
- *4-((2E)-2-(1-amino-3-(4-carboxyphenyl)-1-(hydroxyimino)-3-oxopropan-2-ylidene) hydrazinyl) benzenesulfinate* (*21b*); yield 63% mp:255°C ;IR (KBr) $\nu_{max}/cm^{-1}$: 3,415 (OH), 3,221 (OH), 3,004 ($NH_2$), 1,697 (C=O), 1,653 (C=O); $^1$HNMR (DMSO-$d_6$): 2.5 (s, 1H, *H*O $D_2O$ exchangeable), 6.25–7.3 (m, 4H),7.5 (s, 1H, *H*N, $D_2O$ exchangeable), 8.0–8.1 (m, 4H), 8.5 (s,2H, $H_2ND_2O$ exchangeable), 11.8 (s, 1H, *H*O $D_2O$ exchangeable); m/z: 389 ($M^+$, 100.0%); anal calcd $C_{16}H_{13}N_4O_6S$ (389.36) C, 49.36; H, 3.37; N, 14.39; S 8.24%; found: C, 49.33; H, 3.34; N, 14.36; S 8.28%.
- *4-((2E)-3-amino-2-(2-(4-fluorophenyl)hydrazono)-3-(hydroxyimino)propanoyl) benzoic* acid (21c) Yield 55% mp:2700 C IR (KBr) $\nu_{max}/cm^{-1}$: 3,415 (OH), 3,221 (OH), 3,004 ($NH_2$), 1,697 (C=O), 1,653 (C=O); $^1$HNMR (DMSO-$d_6$): 2.5 (s,1H, *H*O $D_2O$ exchangeable), 6.25–7.3 (m, 4H), 7.5 (s, 1H, *H*N, $D_2O$ exchangeable), 8.0–8.1 (m, 4H), 8.5 (s, 2H, $H_2N$, $D_2O$ exchangeable), 11.8 (s, 1H, *H*O $D_2O$ exchangeable); m/z: 344($M^+$, 100.0%); anal calcd $C_{16}H_{13}FN_4O_4$ (344.09) C, 55.82; H, 3.81; N, 16.27; F 5.52%; found: C, 55.85; H, 3.83; N, 16.25; F 5.55%.

### *2.1.16 General method for reaction of compounds (21a-c) with triethyl amine*

A mixture of equimolar amount of compound *21a*, *b* and *d* and triethyl amine in (10 ml) dimethyl formamide DMF was heated under reflux for 1 h. The reaction mixture was left to cool to room temperature. The solid product so-formed was filtered and crystallised from ethanol.

4-(5-amino-2-(4-bromophenyl)-2H-1,2,3-triazole-4-carbonyl)benzoic acid (*22a*) yield 52% mp:253°C, IR (KBr) $\nu_{max}/cm^{-1}$: 3,350 (OH), 3,206–3,010 ($NH_2$), 1,705 (C=O),

1,596 (C=O), $^{1}$HNMR (DMSO-$d_6$): 7.3–7.4 (m, 4H), 7.5 (s, 2H, $H_2$N, $D_2O$ exchangeable), 7.8–7.9 (m, 4H), 12.5 (s, 1H, HO $D_2O$ exchangeable); $^{13}$C NMR (DMSO-$d_6$): 123, 129, 130, 132, 134, 138, 140, 169, 189; MS (m/z): 386 ($M^+$, 100.0%), 205 (58.5%), 387 (0.04%); anal calcd $C_{16}H_{11}Br\ N_4O_3$ (387.19) C, 49.63; H, 2.86; N, 14.47; Br 20.64%; found: C, 49.65; H, 2.88; N, 14.45; Br 20.66%.

*4-*(*4-amino-5-*(*4-carboxybenzoyl*)*-2H-1,2,3-triazol-2-yl*)*benzene sulfinate* (*22b*) yield 59% mp: 280°C; IR (KBr) $v_{max}/cm^{-1}$: 3,350 (OH), 3,210–3,017 ($NH_2$), 1,705 (C=O), 1,596 (C=O); $^{1}$HNMR (DMSO-$d_6$): 7.4–7.5 (m, 4H), 7.7 (s, 2H, $H_2N$, $D_2O$ exchangeable), 7.8–8.05 (m, 4H), 12.5 (s, 1H, *H*O $D_2O$ exchangeable); m/z: 93($M^+$, 100.0%), 370 (0.05%), 228 (25.5%); anal calcd $C_{16}H_{11}\ N_4O_5S$ (371.35) C, 51.75; H, 2.99; N, 15.09; S 8.63%; found: C, 51.77; H, 2.98; N, 15.06;S 8.66%.

*4-*(*5-amino-2-*(*4-fluorophenyl*)*-2H-1,2,3-triazole-4-carbonyl*)*benzoic acid* (*22c*); yield 60% mp: 2,400 C, IR (KBr) $v_{max}/cm^{-1}$: 3,716 (OH), 3,653–3,202($NH_2$), 1,683 (C=O), 1,636 (C=O), $^{1}$HNMR (DMSO-$d_6$): 7.3–7.4 (m, 4H), 7.5 (s, 2H, $H_2N$, $D_2O$ exchangeable), 7.8–7.9 (m, 4H), 12.5 (s, 1H, *H*O $D_2O$ exchangeable); m/z: 326 ($M^+$, 100.0%); anal calcd $C_{16}H_{11}F\ N_4O_3$ (326.28) C, 58.90; H, 3.40; N, 14.71; F 5.82%; found: C, 58.91; H, 3.42; N, 14.72; F 5.83%.

## *2.2 Biological screening*

### *2.2.1 Antimicrobial activity*

Antibacterial and antifungal activities were done at the Regional Centre for Mycology and Biotechnology (RCMB), Alazhar University, Cairo, Egypt. Initially, target compounds were evaluated in vitro for their antibacterial and antifungal activity, by inhibition zone technique using Four fungi: A. fumigatus (RCMB 02568, Af), Candida albicans (RCMB 05036,Ca), Syncephalastrum racemosum (RCMB, 016001, Sr) and Geotricum candidum(RCMB,052006 Gc), two Gram positive bacteria: S. pneumonia (RCMB 010010,Sp) and B. subtilis (RCMB 010069, BS), two Gram-negative bacteria: E. coli (RCMB 010052, Ec) and Neisseria gonrrhoeae ( NCCP11945, Ng), Suspension of the above-mentioned microorganisms was prepared by inoculating fresh stock cultures into separate broth tubes, each containing 7 ml of nutrient broth (pepton,0.3%) beef extract (0.3%). The inoculated tubes were incubated at 37°C for 24 h. The tested compounds and reference drugs. Solutions of the tested compounds and reference drugs were prepared by dissolving 0.5 g of the compound in 10 ml DMF (Andrews, 2001).

### *2.2.2 Antioxidant activity:*

Organic acids and esters compounds (Kostova and Saso, 2013; Al-Dhabi et al., 2015) and *P*-heterocycles in particular (Morimoto et al., 1995) have been recognised as antioxidant activity. Furthermore, their mechanism of action and the structure-activity relationships (SAR) were extensively studied. DPPH (2,2-diphenyl-1-picryl-hydrazyl-hydrate) free radical method is an antioxidant assay based on electron-transfer that produces a violet solution in ethanol. Stable free radical, at room temperature, which reduced in the presence of an antioxidant molecule, giving rise to colourless ethanol solution. The use of the DPPH assay provides an easy and rapid way to evaluate antioxidants by spectrophotometry, so it can be useful to assess various products at a time. Lack evidence solution can be more effective as an antioxidant or even if there are other solutions with

equal or more capacity to eliminate free radicals from dental surfaces after bleaching procedures, the purpose of this study was to evaluate the antioxidant activity of several agents proposed for reversion of problems caused by bleaching procedures using the DPPH free radical assay. Antioxidant percentage activity of (AA%) of each substance was assessed by DPPH free radical assay. The measurement of the DPPH radical scavenging activity was performed according to methodology described via (Brand-Williams et al., 1995). The stable DPPH radical reacted with samples in an ethanol solution. The reaction mixture consisted of adding 0.5 ml of sample, 3 ml of absolute ethanol and 0.3 ml of DPPH radical solution 0.5 mM in ethanol. When DPPH reacts with an antioxidant compound, which can donate hydrogen, it is reduced. The changes in colour (from deep violet to light yellow) were read [absorbance (Abs)] at 517 nm after 100 min of reaction using a UV/VIS spectrophotometer (DU 800; Beckman Coulter, Fullerton, CA, USA). The mixture of ethanol (3.3 ml) and sample (0.5 ml) serve as blank. The control solution was prepared by mixing ethanol (3.5 ml) and DPPH radical solution (0.3 ml). The scavenging activity percentage (AA%) was determined according to (Mensor et al., 2001).

## 3 Results and discussion

### *3.1 Chemistry*

Sun degradation of PET plastic waste using NaOH solution for five weeks afforded the corresponding terephthalic acid (1) in 90% fruit, followed by esterification in dry butanol containing $H_2SO_4$ to afford a mixture of di-butyl terephthalate *2a* (80%) and 4-(butoxycarbonyl) benzoic acid *2b* (10%) (Fahim et al., 2016) (Figure 1).

4-Butyrylbenzohydrazide (*3*) was prepared by the reaction of dibutyl-terephthalte (*2a*) with hydrazine hydrate in equal ratio (1:1) in ethanol (Figure 1). 4-Butylrylbenzohydrazide (*3*) was allowed to react with carbon disulfide; in ethanol in the presence of KOH to give the corresponding thiocarbonate salt *4*. When the salt *4* was treated by hydrazine hydrate it a give the corresponding 4-(5-mercapto-4-amino-1,3, 4-triazole) benzoic acid (*5*) (Figure1). The construction of the latter product was built on the foundation of its elemental analysis and spectral data which are compatible with the specified structure. For instance, its mass spectrum revealed a molecular ion peak at m/z 236 (cf. *experimental part*). 4-(5-mercapto-4-amino-1,3,4-triazole) benzoic acid (*5*) also reacted with different aromatic aldehydes; in refluxing ethanol and in the bearing of a catalytic amount of piperidine; to give the corresponding amines *6a*, *b* as outlined in Figure 1.

The IR spectra of the latter products showed, in each instance, the appearance of OH, NH absorption band in the region 3,230–3,121 $cm^{-1}$ and showed CH=N- proton signal near δ 10.9 in their $^1H$ NMR spectra. Reaction of compound 5 with 2-aminobenzenethiol in the presence of $POCl_3$ afforded a product identified as 4-amino-5-(4-(benzothiazol-2-yl) phenyl)-4*H*-1,2,4-triazole-3-thiol *7* (Figure 1). The IR spectrum of the reaction product exhibited NH2 absorption band 3,873 $cm^{-1}$. Its $^1H$ NMR spectrum showed singlet signal δ 13.7 corresponding to SH proton. The mass spectrum of the product *7* revealed a peak at m/z 325 corresponding to its molecular ion. In a like fashion, when compound *5* was treated with methyl iodide in potassium hydroxide solution to afford 4-(4-amino-5-(methylthio)-4H-1,2,4-triazol-3-yl) benzoic acid (*8*). The latter product reacted with ethyl

bromoacetate to afford 4-(4-amino-5-(2-ethoxy-2-oxoethylthio)-4*H*-1,2,4-triazol-3-yl) benzoic acid (*9*). The structure of the obtained product was supported on the base of its spectral information. For exemplar, the IR spectrum of compound 9 exhibited bands at 3,426, 1,741 and 1,632 $cm^{-1}$ characteristics for NH2 and two C=O groups, respectively.

**Figure 1** (a) Degradation of PET and synthesis of amino-1,3,4-triazole derivative 5
(b) Reaction of compound 5 with (1) aromatic aldehydes; (2) 2-aminobenzenethiol and (3) ethyl bromoacetate

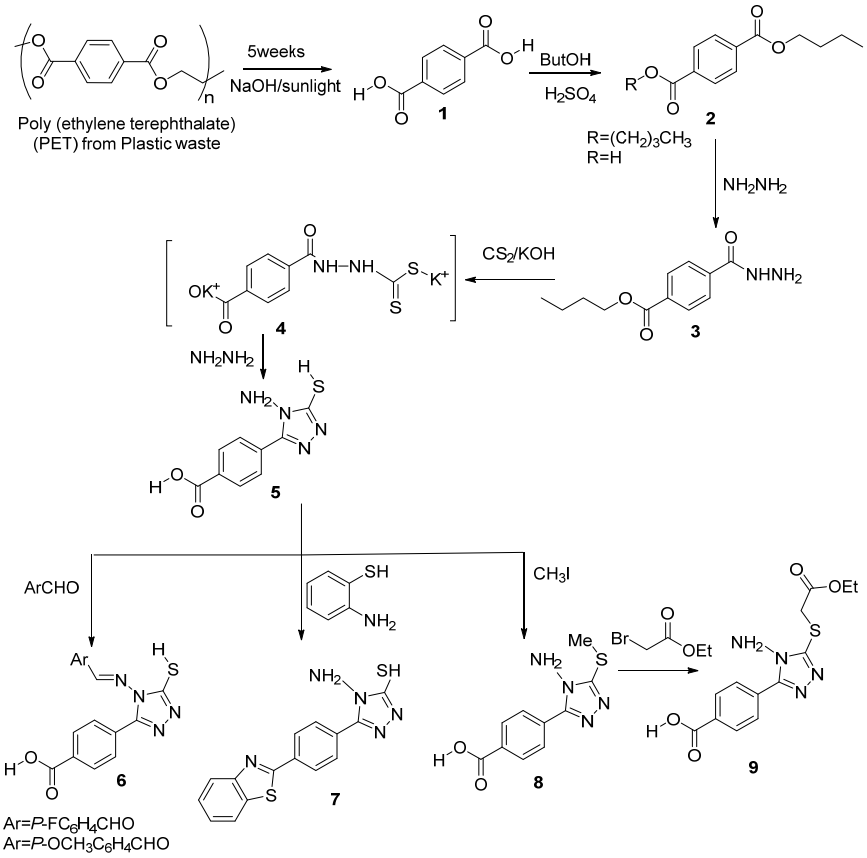
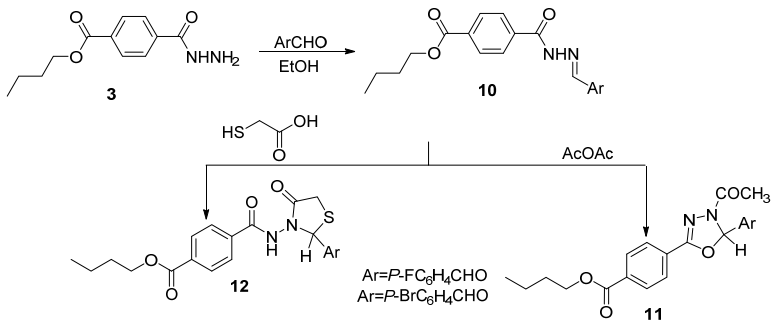
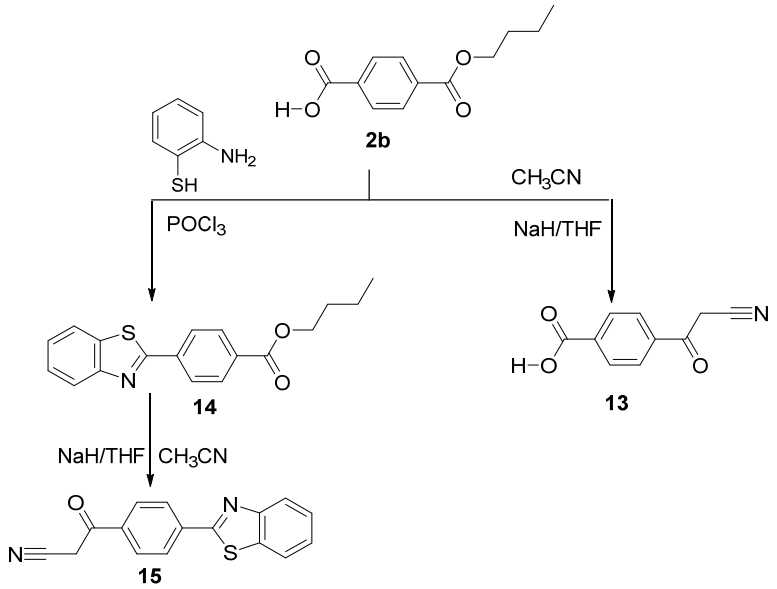



**Figure 2** Reaction of hydrazones derivatives*10* with glacial acetic acid and thioglycolic acid



The response of the benzohydrazide *3* with aromatic aldehydes in ethanol; afforded the corresponding hydrazones *10a*, *b* (Figure 2). The IR spectrum of compound *10a*, taken as a typical case of the series; exhibited two strong carbonyl bands in 1,719 and 1,648 $cm^{-1}$ in addition to NH band at 3,262 $cm^{-1}$. The 1H NMR spectrum of 10 a revealed $D_2O$-exchangeable signal at δ 11.99 due to amide proton and its δ 8.6 due to a methine proton, in addition to an aromatic multiplet at δ 7.21–7.42. When compound *10a* was relaxed in glacial acetic acid it afforded the corresponding 1-(4-(4-acetyl-5-(4-fluorophenyl)-4,5-dihydro-1,3,4-oxadiazol-2-yl)phenyl) benton-1-one *11a*. (Figure 2). Besides; the reactivity of hydrazones 10b towards thioglycolic acid was also investigated which afforded oxothiazolidin-3-ylcarbamoyl) benzene derivatives *12b*. The constructions of the latter products were designated on the ground of their analytical and spectral information. Hence, The IR spectra of the reaction products showed in each case; carbonyl absorption band in the region 1,719–1,650 $cm^{-1}$. Their mass spectra revealed molecular ion peaks at the appropriate m/z value 476 (*cf. experimental part*).

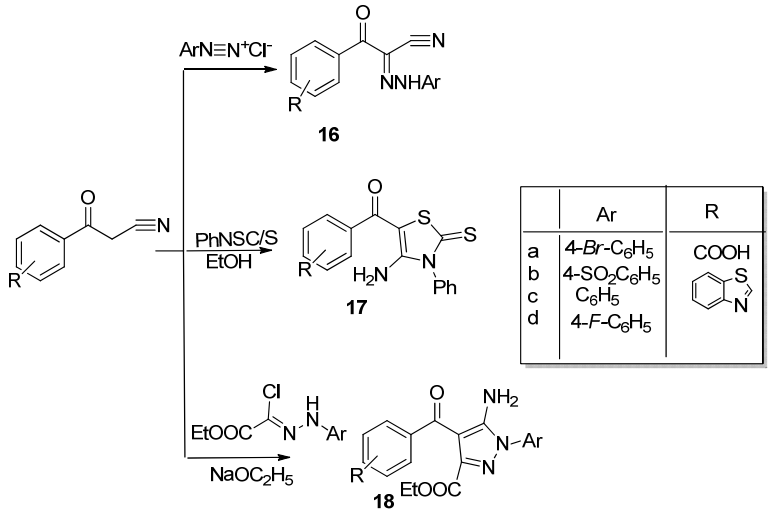
**Figure 3** Synthesis of 3-Oxo-3-phenylpropanenitrile derivatives *13* and *15*




When 4-pentanoylbenzoic acid (*2b*) was treated with acetonitrile, in the presence of sodium hydride, followed by acidification with HCl, it furnished a single product identified as 4-(2-cyanoacetyl)benzoic acid (*13*) as depicted in Figure 3. On the other hand, 1*H*-benzo [*d*] [1,2,3] triazol-1-yl-4-(benzo [*d*] thiazol-2-yl)benzoate (*14*) was readily obtained, in good yield, *via* the reaction of 4-pentanoylbenzoic acid (*2b*) with 2-aminobenzenethiol, in the presence of $POCl_3$ as shown in Figure 3. The structure of compound *14* was confirmed on the basis of its elemental analysis and spectral data. For example, its IR spectrum showed a strong carbonyl absorption band at 1,722 $cm^{-1}$. Its $^1H$ NMR spectrum revealed triplet signals at δ 0.95 (J = 0.05) due to methyl proton and multiplet signal at δ 4.33 (J = 12.95) due ($OCH_2$ proton) in addition to multiplet signal in the region 7.8–8.1 ppm due to aromatic protons, respectively. The mass spectrum of compound *14* revealed a peak at m/z 311 corresponding to its molecular ion. When

compound *15* was treated with acetonitrile in the presence of sodium hydride, it furnished 3-(4-(benzothiazol-2-yl)phenyl)-3-oxopropanenitrile (*15*) (Figure 3) the structure of compound *15* was constructed along the basis of its spectral data (*c.f. experimental*).

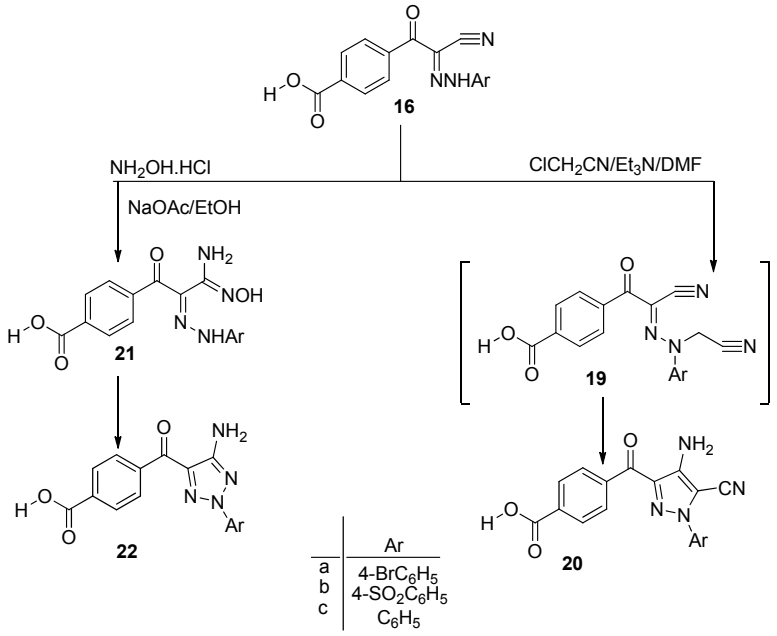
**Figure 4** Reactions of 3-Oxo-3-phenylpropanenitrile derivatives *13* and *15*




3-Oxo-3-phenylpropanenitrile derivatives *13* and *15* couple smoothly with aryan diazonium salts to give the corresponding hydrazone derivatives *16*; respectively (Figure 4). The IR spectra of the isolated products revealed, in each example, the absorption band near 2,210 $cm^{-1}$ due to nitrile group and NH absorption band near 3,233 $cm^{-1}$. The $^1H$ NMR spectrum of compound *16a*, taken as a typical model of the serial publication, revealed $D_2O$-exchangeable signal at δ 10.5 due to hydration NH proton.

Treatment of 3-Oxo-3-phenylpropanenitrile derivatives *13* and *15* with elemental sulfur and phenyl isothiocyanate, in ethyl alcohol containing a catalytic amount of triethylamine, afforded 4-amino-3-phenyl-2-thioxo-2,3-dihydrothiazol-5-yl)phenyl) methanone derivatives *17*; respectively (Figure 4). The reactivity of compounds *13* and *15* toward hydrazonyl halides was investigated. Thus discussion of *13* and *15* with hydrazonyl halides in ethanolic sodium ethoxide solution, given the corresponding pyrazole derivatives *18* (Figure 4). The elemental analysis and spectral data were in complete conformity with the amino-pyrazole structures *18*. For exemplar, the IR spectrum of the product *18* a showed absorption bands at 3,346 $cm^{-1}$ and 3,219 $cm^{-1}$ due to amino group and revealed the broad band at 3,426 due to the OH group in addition to three bands due to carbonyl groups in 1,716, 1,642 and 1,602 $cm^{-1}$, respectively. Moreover, it is $^1H$ NMR spectrum revealed $D_2O$-exchangeable signal at δ 7.35 corresponding to $NH_2$ protons (*cf. experimental part*).

**Figure 5** Reactions of hydrazines *16a–c* with chloroacetonitrile and hydroxylamine hydrochloride




The hydrazines *16a–c* were reacted with chloroacetonitrile; in ethanol and in the bearing of a catalytic amount of triethylamine to produce the corresponding pyrazole derivatives *20* (Figure 5). The hydrazones *16a–c* were allowed to react also with hydroxylamine hydrochloride in the presence of sodium acetate to yield amidoximes *21a–c* (Figure 5). The latter intermediates underwent intramolecular cyclisation to yield the corresponding aminotriazole derivatives *22a–c*. The constructions of the new triazole derivatives *16a–c* have been elucidated by elemental analyses, $^1$H NMR for *22* by taking as a typical example; revealed $D_2O$-exchangeable signal due to amino group protons at δ 7.5 and a signal at δ 12.5 corresponding to the OH proton. The IR spectrum of compound *22b* showed a vibration absorption band at 3,350 $cm^{-1}$ attributable to OH group. The two vibrational bands at 3,206 and 3,010 $cm^{-1}$ were assigned to the asymmetric and symmetric stretching vibration bands of the $NH_2$ group.

## *3.2 Anti-microbial activity*

The results, depicted in Table 1 revealed the most of the tested compounds displayed variable inhibitory effects on the growth of G+ and G– bacterial strain and four antifungal strains. In general, we could concluded that, the tested compounds showed moderate antibacterial activity when compared with the reference drug and low weak antifungal activity, when compared with the reference drug. It is worth to mention that *6a*, *b*, *16a*, *16b*, *16d*, *20a* and *22a* shows high activity against all types of strains, compounds *3*, *11*, *12* and *22d* show moderate activity against all strains, All the tested compounds were reflecting no inhibition of growth against *Pseudomonas aeruginosa* (*G–*) and *Candida albicans* (Cushnie and Lamb, 2005).

**Table 1** The antimicrobial activity screening of the prepared compounds at concentration 2 mg/disc compared with amphotericin B and ampicillin and gentamicin as a reference drugs

| *Sample ID* | *Antibacterial, antifungal activity in mm/conc1mg/ml*$^{-1}$ ) | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | *Bacillus subtiles(G+) Bs* | *Streptococcus peneumoniae (G+) Sp* | *Escherichia coli (G–) Ec* | *Pseudomonos aeruginosa (G–) Pa* | *Asperglus flavus (Fungus) Af* | *Candida albicans (Fungus) Ca* | *Syncephalastrum racemosum (Sr)* | *Geotricum candidum (Gc)* |
| 3 | 16.1±0.24 | 15.1±0.20 | 16.1±0.24 | NA* | 21.0± | NA | 18.2±0.23 | 15.2±0.22 |
| 5 | 17±0.26 | 16±0.25 | 20.2±0.30 | NA | NA | NA | 18.2±0.22 | NA |
| 6a | 17.2±0.27 | 15.2±0.36 | 11.4±0.36 | NA | 14.2±0.39 | NA | 11.3±0.58 | 15.2±0.19 |
| 6b | 17.2±0.27 | 15.2±0.36 | 10.8±0.33 | NA | 13.4±0.25 | NA | 10.6±0.58 | 14.4±0.17 |
| 7 | 24.2±0.25 | 22.3±0.34 | 17.4±0.58 | NA | 20.9±0.63 | NA | 17.6±0.27 | 25.4±0.35 |
| 11 | 11.1±0.30 | 13.0±0.25 | 12.1±.020 | NA | NA | NA | 12.2±0.25 | NA |
| 12 | 12.2±0.20 | 11.1±0.22 | 11.2±0.15 | NA | NA | NA | 12.2±0.19 | NA |
| 16a | 20.8±0.58 | 19.5±0.44 | 15.3±0.19 | NA | 16.7±0.25 | NA | 15.6±0.25 | 18.2±0.58 |
| 16b | 21.6±0.25 | 20.8±0.34 | 16.2±0.58 | NA | 19.7±0.63 | NA | 15.2±0.27 | 22.4±.35 |
| 16c | 14.7±0.27 | 11.1±0.36 | 9.3±0.36 | NA | 10.3±0.39 | NA | 9.2±0.58 | 11.2±0.19 |
| 16d | 18.3±0.25 | 15.6±0.36 | 12.9±0.36 | NA | 15.3±0.39 | NA | 12.9±0.58 | 17.4±0.19 |
| 20a | 20.2±0.25 | 19.3±0.34 | 15.7±0.58 | NA | 18.2±0.63 | NA | 17.1±0.27 | 20.6±0.35 |
| 20b | 14.7±0.25 | 10.3±0.44 | 12.9±0.39 | NA | 12.3±0.55 | NA | 10.1±0.25 | 12.9±0.58 |
| 20c | 18.9±0.25 | 17.3±0.34 | 16.3±0.19 | NA | 16.3±0.63 | NA | 13.9±0.27 | 19.2±0.35 |
| 22a | 19.8±0.63 | 15.7±0.44 | 15.6±0.25 | NA | 10.6±0.39 | NA | 9.3±0.58 | 13.4±0.58 |
| 22b | 19.6±0.25 | 18.1±.55 | 17.4±0.19 | NA | 17.3±0.44 | NA | 14.4±0.25 | 19±0.58 |
| 22d | 16.3±0.27 | 12.2±0.36 | 10.8±0.36 | NA | 12.6±0.39 | NA | 10.4±0.58 | 13.6±0.19 |
| Amphotericin B | - | - | - | - | 23.7±0.1 | 19.7±0.2 | 28.7±0.2 | 25.4±0.1 |
| Ampicillin | 32.4±0.3 | 23.8±0.2 | - | - | - | - | - | - |
| Gentamicin | - | - | 19.9±0.3 | 17.3±0.1 | - | - | - | - |

Notes: NA*: No activity; the screening organisms, mould: Gram positive bacteria: *B. subtilis* (RCMB 010069, Bs) and *S. pneumonia* (RCMB 010010, Sp), two Gram-negative bacteria: *E. coli* (RCMB 010052, Ec) and *Neisseria gonrrhoeae* (NCCP11945, Ng), Four fungi *A.fumigatus* (RCMB 02568, Af), *Candida albicans* (RCMB 05036, Ca) *Syncephalastrum racemosum* (RCMB, 016001, Sr) and *Geotricum candidum* (RCMB,052006, Gc), inhibition zone : high activity > 15 (mm), moderate activity 11–14 (mm), slight activity 8–10 (mm) and non-sensitive 0–7 (mm.)

We then investigated the effect of attaching different non fused five-member rings to benzoic acid derivatives *5*, *6a*, *6b*, *16a–d*, *20a–c* and *22a, b* and *d*) and 2-phenylbenzothiazole derivatives *7*, and 4-ethyl benzoate cores (derivatives *11* and *12*). Generally, acid derivatives *16a–d*, *20a–c* and *22a*, *b* and *d*, also benzothiazole derivatives *7* showed better antibacterial activities than the esterified members *11* and *12*, Also, incorporation of substituted 1,3,4-triazole moiety in compound *7* resulted in a good antibacterial activity against Gram negative bacteria. Moreover, compound *7* bearing substituted 1,3,4-oxadiazole moiety emerged as the most active member against Gram positive *B. subtilis* (24.2±0.25 mg/ml$^{-1}$) and fungus *G. candidum* (25.4±0.35 mg/ml$^{-1}$) among its benzothiazole analogous and in this study. On the other hand, incorporation of hydrazone derivatives with the benzoic acid core led to compounds *16a–d*, respectively. Compound *16b* (21.6±0.25 mg/ml$^{-1}$) was more potent than (20.8±0.58 mg/ml$^{-1}$) against all tested Gram positive, Gram negative bacteria and antifungal activity against C. albicans.

## *3.3 DPPH radical scavenging*

Compounds *2a*, *3*, and *9* exhibited good radical scavenging ability as compared to standard ascorbic acid (34 μM ±6.17), whereas compounds *3* and *6b* displayed moderate radical scavenging activity. However, the starting compound *13* showed minimum activity. Furthermore, [4-(4-amino-5-(2-ethoxy-2-oxoethylthio)-4H-1,2,4-triazol-3-yl) benzoic acid (*9*) (48.8 μM ±10.5) is demonstrated high radical scavenging activity is demonstrated high radical scavenging activity in the micro-molar range, and a number of these also proved potent in the low micro-molar range due to the presence of OH group and also and di-butyl terephthalate *2a* (47.1 μM ±10.34) exhibited high antioxidant activity. This widely used method determines antioxidant activity by measuring the hydrogen donating ability of the compound being studied. IC50 values are displayed in Table 2.

**Table 2** DPPH radical scavenging of new synthesised compounds

| *Sample ID* | *Absorb./ samples (A)* | *Inhibition%* | *DPPH $IC_{50}$ (μM)*[a] |
|---|---|---|---|
| Vitamin C | 0.07 | 89.55% | 34.01±6.17[b] |
| 2a | 0.15 | 66% | 47.1±10.34 |
| 2b | 0.31 | 59.8% | 68.34±10 |
| 3 | 0.28 | 62.3% | 58±16.25 |
| 22 | 0.21 | 63.6% | 66.06±0.525 |
| 6b | 0.23 | 60% | 56.64±16.6 |
| 7 | 0.27 | 64.5% | 59.34±3.32 |
| 9 | 0.18 | 69.9% | 48.8±10.5 |
| 13 | 0.20 | 67.9% | 90.34±2.46 |
| 15 | 0.21 | 67.09% | 66.9±2.4 |
| 16a | 0.31 | 61.9% | 71.6±5.1 |
| 17 | 0.13 | 70.9% | 68.76±2.59 |
| 22 | 0.27 | 67.5% | 71.72±13.2 |
| 20a | 0.25 | 62.3% | 76.48±2.58 |
| 20d | 0.26 | 62.2% | 65.78±2.08 |

Notes: [a]IC50 values represent as mean ± SD of three determinations and [b]Reported IC50 = 15.3μM.

Vitamin C was used as a positive standard for the antioxidant activity in all experiments. antioxidant assay by ABST method % inhibition% = {[A sample – A test] / A control} × 100, the data presented in Table 2, showed that all new synthesised compounds showed good to moderate antioxidative activity. Nevertheless, N,S,O-heterocycles *2a*, *3* and *9* exhibited good radical scavenging ability as compared to standard ascorbic acid (34.41%), whereas compounds *6b* displayed moderate radical scavenging activity. However, the starting compound *13* showed minimum activity (90.34 µM ±24.6). Furthermore, 4-(4-amino-5-(2-ethoxy-2-oxoethylthio)-4H-1,2, 4-triazol-3-yl)benzoic acid (*9*) (48.8 µM ±10.5) is demonstrated high radical scavenging activity in the micro-molar range due to radical scaverange of hydroxyl moiety, and a number of these also proved potent in the low micro-molar range due to the presence of OH group and also and di-butyl terephthalate *2a* (47.1 µM ±10.34) exhibited high antioxidant activity.

## 4 Conclusions

Sun degradation of poly (ethylene terpthalte) is green environmentally which used for synthesis of series of new pyrazole, triazole, oxadiazole and hydrazone heterocycles, the synthesised compounds were evaluated for in vitro antibacterial activity and antioxidant activity. The SAR study displayed in Table 1 and 2 showed that the synthesised antibacterial activity of benzoic acid *7* resemble that of the known parapenes preservative which are useful in industrial applications, On the other hand the activity of the 1,2,4-triazole *16b* show higher activity against all types of strains. Also compounds of dibutyl-terephthalte (*2a*) and 4-(4-amino-5-(2-ethoxy-2-oxoethylthio)-4H-1,2,4-triazol-3-yl) benzoic acid (*9*) exhibited high antioxidant activity due to presence of OH group. It can be concluded that this class of compounds certainly holds great promise towards pursuit to discover novel class of antimicrobial and antioxidant agents. Further studies are being conducted to acquire more information about quantitative structure-activity relations.

## References

Abu-Zaied, M., El Telbanie, E.M., Elgemhie, G. and Nawwar, G.A.M. (2011) 'Synthesis and in vitro anti-tumor activity of new oxadiazole thioglycosides', *European Journal of Medicinal Chemistry*, Vol. 46, pp.229–235.

Al-Dhabi, N.A., Arasu, M.V. and Rejiniemon, T.S. (2015) 'In vitro antibacterial, antifungal, antibiofilm, antioxidant, and anticancer properties of isosteviol isolated from endangered medicinal plant *Pittosporum tetraspermum*, *Evid Based Complement Alternat Med.*, 11pp, Article ID 164261.

Al-Salem, S.M., Lettieri, P. and Baeyens, J. (2009) 'Recycling and recovery routes of plastic solid waste (PSW): a review', *Waste Management*, Vol. 29, No. 10, pp.2625–2643.

Andrews, J.M. (2001) 'Determination of minimum inhibitory concentrations', *Journal of Antimicrobial Chemotherapy*, Vol. 48, Suppl. 1, pp.5–16.

Brand-Williams, W., Cuvelier, M.E. and Berset, C. (1995). 'Use of free radical method to evaluate antioxidant activity', *Lebensmittel Wissenschaft and Technologie*, Vol. 28, No. 1, pp.25–30.

Chenot, E-D. (2007) 'Preparation of monoalkyl terephthalatesan overview', *Synthetic Communications*, Vol. 37, No. 3, pp.483–490.

Cushnie, T.P.T. and Lamb A.J. (2005) 'Antimicrobial activity of flavonoids', *International Journal of Antimicrobial Agents*, Vol. 26, No. 5, pp.343–356.

Daniel, P. and Tadeusz, S. (1997) 'Chemical recycling of PET', *Indian Engineering Chemistry Research*, No. 36, p.1373.

Dawood, K.M. and Farag, A.M. (1998) 'Heterocyclic synthesis via enaminonitriles: one- pot synthesis of some new pyrazole, isoxazole, pyrimidine, pyrazolo[1,5-a]pyrimidine pyrimido[1,2-a]benzimidazole and pyrido[1,2-a]benzimidazole derivatives', *Journal of Chemical Research*, No. 4, p.208–209.

Dawood, K.M., Farag, A.M. and Abdel-Aziz, H.A. (2005) 'Synthesis and antimicrobial evaluation of some 1,2,4-triazole, 1,3,4-oxa(thia)diazole, and 1,2,4-triazolo[3,4-b]-1,3,4-thiadiazine derivatives', *Heteroatom Chemistry*, Vol. 16, No. 7, pp.621–627.

EI-Fattah, M.E.A., (1998) 'A novel synthesis of heterocyclic compounds containing coumarin moiety of potential antimicrobial activity', *Archive Pharma. Research*, Vol. 21, No. 6, pp.723–728.

Fahim, A.M. (2017a) 'Microwave assisted regioselective synthesis and biological activates of pyrano[2,3-c]pyridine derivatives utilizing DMAP as a catalyst', *Online Journal of Biological Sciences*, Vol. 17, No. 4, pp.39–404.

Fahim, A.M. (2017b) 'Regioselective synthesis of novel fused sulphonamide derivatives utilizing microwave irradiation', *Current Microwave Chemistry*, Vol. 4, pp.1–9.

Fahim, A.M., Farag, A.M. and Nawwar, G.A.M. (2013) 'PET waste recycling as chemical feedstock: synthesis and antimicrobial activity of new compounds with anticipated industrial use', *Journal of Applicable Chemistry*, Vol. 2, No. 3, pp.502–510.

Fahim, A.M., Farag, A.M., Yakout, E.S.M.A., Nawwar, G.A.M. and Ragab, E.A. (2016) 'Synthesis, biological evaluation of 1,3,4-oxadiazole, triazole and uracil derivatives from poly (ethylene terephthalate) waste', *Egypt. J. Chem.*, Vol. 59, No. 3, pp.285–303.

Fahim, A.M., Yakout, E.S.M. and Nawwar, G.A. (2014) 'Facile synthesis of in-vivo insecticidial and antimicrobial evaluation of bis heterocycle moiety from PET waste', *Online Journal of Biological Sciences*, Vol. 14, No. 3, pp.196–208.

Fahim, A.M., Zayed, E.A., Mohamed, A., Zayed, M.A. and El-Samahy, F.A. (2017) 'Novel macrocyclic Schiff base and its complexes having $N_2O_2$ group of donor atoms: synthesis, characterization and anticancer screening', *Appl. Organometal Chem*., Vol. 31, p.e3694.

Fahim, A.M., Farag, A.M., Rabie, M.S. and Ragab, E.A. (2018) *European Journal of Chemistry*, Vol. 9, No. 1, pp.30–38.

Gürsoy, A. and Karali, N. (2003) 'Synthesis and primary cytotoxicity evaluation of 3-[[(3-phenyl-(3H)-quinazolinone-2-yl)mercaptoacetyl]hydrazono]-1H-2-indolinones', *European Journal of Medicinal Chemistry*, Vol. 38, No. 6, pp.633–643.

Husain, A. and Naseer, M.A. (2011) 'Studies on fused heterocyclic 3,6-disubstituted-1,2, 4-triazolo-1,3,4-thiadiazoles: synthesis and biological evaluation', *Medicinal Chemistry Research*, Vol. 20, No. 1, pp.47–54.

Kawamura, C., Ito, K., Nishida, R., Yoshihara, I. and Numa, N. (2002) 'Coating resins synthesized from recycled PET', *Progress in Organic Coatings*, Vol. 45, Nos. 2–3, pp.185–191.

Kostova, I. and Saso, L. (2013) 'Advances in research of schiff-base metal complexes as potentantioxidants', *Current Medicinal Chemistry*, December, Vol. 20, No. 36 pp.4609–4632.

Krzysztof, W., Cebak, A.W. and Joanna, G. (2003) 'Direct dyes derivedfrom iso- and terephthalic acids', *Dyes and Pigments*, Vol. 56, No. 2, pp.99–109.

Lian-Chun, H., Oku, A., Yamada, E. and Tomari, K. (1997) 'Alkali-decomposition of poly(ethylene terephthalate) in mixed media of non-aqueous alcohol and ether, study on recycling of poly(ethylene terephthalate)', *Journal of Applied Polymer Science*, Vol. 63, p.595–601.

Mensor, L.L., Menezes, F.S., Leitão, G.G., Reis, A.S., dos Santos, T.C., Coube, C.S. and Leitão, S.G. (2001) 'Screening of Brazilian plant extracts for antioxidant activity by the use of DPPH free radical method', *Phytother Research*, March, Vol. 15, No. 2, pp.27–30.

Morimoto, Y., Tanaka, K., Iwakiri, Y., Tokuhiro, S., Fukushima, S. and Takeuchi, Y. (1995) 'Erythrocyte hemolysis was mediated by peroxyl radicals in this assay system', *Biol. Pharm. Bull.*, Vol. 18, pp.1417–1422.

Palekar, V.S., Damle, A.J. and Shukla, S.R. (2009) 'Synthesis and antibacterial activity of some novel bis-1,2,4-triazolo[3,4-b]-1,3,4-thiadiazoles and bis-4-thiazolidinone derivatives from terephthalic dihydrazide', *European Journal of Medicinal Chemistry*, Vol. 44, pp.5112–5116.

Ragavan, R.V., Vijayakumar, V. and Kumari, N.S. (2010) 'Synthesis and antimicrobial activities of novel 1,5-diaryl pyrazoles', *European Journal of Medicinal Chemistry*, Vol. 45, pp.1173–1180.

Shiradkar, M.R., Murahari, K.K., Gangadasu, H.R., Suresh, T., Kalyan, C.A., Kaur, D.P.R., Burange, P. and Ghogare, J. (2007) 'Synthesis of new S-derivatives of clubbed triazolyl thiazole as anti-mycobacterium tuberculosis agents', *Bioorganic Medicinal, Chemistry*, Vol. 15, No. 4, pp.3997–4008.

Soural, M., Hlaváč, J., Hradil, P., Fryšová, I., Hajdúch, M., Bertolasi, V. Maloň, M. (2006) 'Synthesis and cytotoxic activity of substituted 2-phenyl-3-hydroxy- 4(1H)-quinolinones-7-carboxylic acids and their phenacyl esters', *European Journal of Medicinal Chemistry*, Vol. 41, No. 4, pp.467–474.

Vicini, P., Incerti, M., Doytchinova, I., La Colla, P., Busonera, B. and Loddo, R. (2006) 'Synthesis and antiproliferative activity of benzo[d]isothiazole hydrazones', *European Journal of Medicinal Chemistry*, Vol. 41, pp.624–632.

Yakout, E.S.M.A., Allam, Y.A., Nawwar, G.A.M. (1999) 'Simple syntheses of benzothiazol-2-ylazoles', *Heteroatom Chemistry*, Vol. 10, No. 3, pp.177–182.

Zhuang, B-R., Hsu, G-J. and Sung, K. (2006) 'A multi-component reaction to 5-cyanouracils: synthesis and mechanistic study', *Bioorganic and Medicinal Chemistry*, Vol. 14, No. 10, pp.3399–3404.