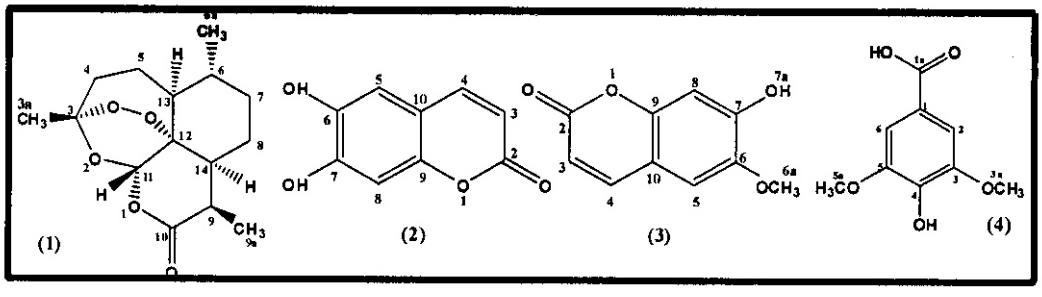
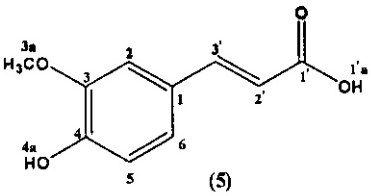
SUMMARY

The present research work includes evaluation of purified compounds isolated from *Artemisia annua, Vitis vinifera, Citrus sinensis, Syzygium aromaticum* and *Curcuma longa* and synthesized thiazolidene-4-one derivatives for their reactive oxygen species (ROS) and xanthine oxidase (XO) inhibitory potential. *A. annua* was subjected to bioassay guided extraction which resulted in the isolation of artemisinine (**1**), aesculetin (**2**) and scopoletin (**3**). Compound **2** was found as the most active XO and ROS inhibitor with IC_{50} value of 72.3 ± 1.3 µM and 99.4 ± 2.6 µM respectively while compounds **1** and **3** exhibited strong ROS and moderate XO inhibition. Syringic acid (**4**) and ferulic acid (**5**) were purified from *V. vinifera* which showed significant XO inhibition potential with IC_{50} value of 81.6 ± 1.3 µM and 67.5 ± 0.3 µM respectively hence both compounds moderately inhibited the reactive oxygen species. Hesperidine (**6**) obtained in major amount from peels of *C. sinensis* exhibited significant ROS and XO inhibition potential with IC_{50} value of 34.8 ± 3.6 µM and 24.3 ± 0.1 µM respectively. *S. aromaticum* yielded eugenol (**7**) and caryophyllene oxide (**8**) by bioassay guided extraction and isolation. The results of ROS and XO assay revealed that both compounds **7** and **8** exhibited significant inhibition with IC_{50} = 84.04 ± 1.1 µM and 57.6 ± 2.7 µM against ROS and IC_{50} = 89.11 ± 0.3 µM and 94.8 ± 2.4 µM against XO respectively. *Trans* cinnamaldehyde (**9**) and curcumin (**10**) were purified from *C. longa* which showed moderate ROS and XO inhibition activity. Compound **6** and **7** were found as active ROS and XO inhibitors. Compound **9** and **10** moderately inhibited the ROS and XO. Compounds **2**, **4** and **5** exhibited strong XO inhibition potential in the order **2** > **5** > **4** hence the compounds **1**, **3** and **8** are strong ROS inhibitors in the order **8** > **3** > **1**.

The synthesized thiazolidene-4-one derivatives were evaluated for ROS and XO inhibition activity and characterized by EI-MS, ^{1}H and ^{13}C-NMR as 3-phenyl-2-thioxothiazolidin-4-one 1,1 dioxide (**11**), (E)-5-benzylidene-3-phenyl-2-thioxothiazolidin-4-one 1,1 dioxide (**12**), (E)-3-phenyl-5-((E)-3-phenylallylidene-2-thioxothiazolidin-4-one 1,1 dioxide (**13**), (E)-5-(2-hydroxybenzylidene)-3-phenyl-2-thioxothiazolidin-4-one 1,1 dioxide (**14**), (E)-5-(4-hydroxy-3-methoxybenzylidene)-3-phenyl-2-thioxothiazolidin-4-one1,1 dioxide (**15**), 2-thioxo-3-*o*-tolylthiazolidin-4-

one c1,1 dioxide **(16)**, (E)-5-benzylidene-2-thioxo-3-*o*-tolylthiazolidin-4-one 1,1 dioxide **(17)**, (E)-5-((E)-3-phenylallylidene)-2-thioxo-3-*o*-tolylthiazolidin-4-one 1,1 dioxide **(18)**, (E)-5-(4-hydroxybenzylidene)-2-thioxo-3-*o*-tolylthiazolidin-4-one 1,1 dioxide **(19)** (E)-5-(4-hydroxy-3-methoxybenzylidene)-2-thioxo-3-*o*-tolylthiazolidin-4-one 1,1 dioxide **(20)**, 3-benzyl-2-thioxothiazolidin-4-one1,1 dioxide **(21)**, (E)-3-benzyl-5-benzylidene-2-thioxothiazolidin-4-one 1,1 dioxide **(22)**, (E)-3-benzyl-5-(4-hydroxy-3-methoxybenzylidene)-2-thioxothiazolidin-4-one 1,1 dioxide **(23)**, 2H –thiazolo[3,2-a]pyrimidine-3,5,7(6H, 8H, 8aH)-trione **(24)**, (Z)-6-benzylidene-2H –thiazolo[3,2-a]pyrimidine-3,5,7(6H, 8H, 8aH)-trione **(25)**, (Z)-6-(4′-chlorobenzylidene)-2H –thiazolo[3,2-a]pyrimidine-3,5,7(6H, 8H, 8aH)-trione **(26)**, (2Z,6E)-2,6-bis(2′-hydroxybenzylidene)-2H –thiazolo[3,2-a]pyrimidine-3,5,7(6H, 8H, 8aH)-trione **(27)**, (Z)-6-(2′-methylbenzylidene)-2H –thiazolo[3,2-a]pyrimidine-3,5,7(6H, 8H, 8aH)-trione **(28)**, (2Z,6E)-2,6-bis(4′-hydroxy-3′-methoxybenzylidene)-2H –thiazolo[3,2-a]pyrimidine-3,5,7(6H, 8H, 8aH)-trione **(29)**, (Z)-6-(4′-methoxybenzylidene)-2H –thiazolo[3,2-a]pyrimidine-3,5,7(6H, 8H, 8aH)-trione **(30)**, (Z)-6-(3′-aminobenzylidene)-2H –thiazolo[3,2-a]pyrimidine-3,5,7(6H, 8H, 8aH)-trione **(31)**, 6-methylene -2H –thiazolo[3,2-a]pyrimidine-3,5,7(6H, 8H, 8aH)-trione **(32)** and (Z)-6-((E)-3′-phenylallylidene)-2H –thiazolo[3,2-a]pyrimidine-3,5,7(6H, 8H, 8aH)-trione **(33)**. The synthesized compounds exhibited strong to moderate ROS and XO inhibition potential with **12** as the most active ROS while **26** as the strong XO inhibitor with IC_{50} value of 43.8 ± 2.1 µM and 62.7 ± 5.1 µM respectively. The compounds **14, 26 and 32** possess significant ROS and XO inhibition while the order of strong and moderate ROS inhibitors is **12 > 32 > 29 > 24> 26 > 11 > 15 > 17 > 33 > 19 > 25 > 14 > 23** and **18 > 31 > 16 > 13 > 20 > 22 > 27 > 28** respectively. Therefore the order of strong XO active compounds is **26 > 32 > 30 > 14** hence the order of moderately active XO compounds is **27 > 31 > 17 > 33 > 23 > 13 > 22 > 12 > 21 > 18 > 16 > 25**.





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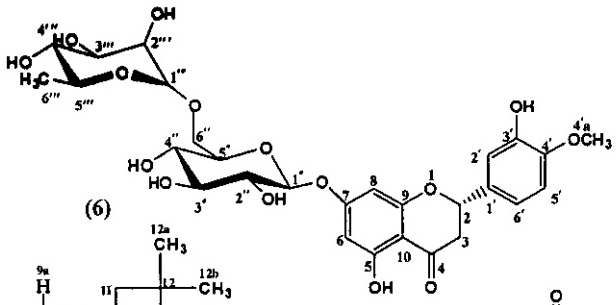

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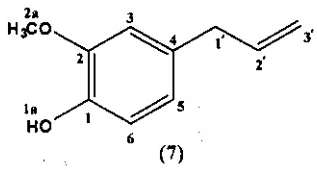

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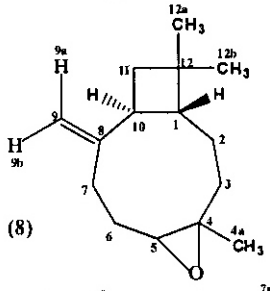

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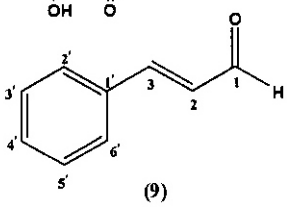

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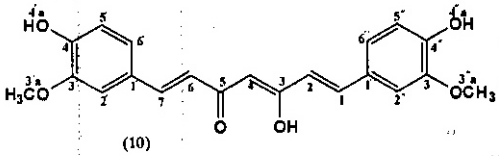

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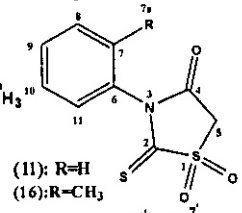
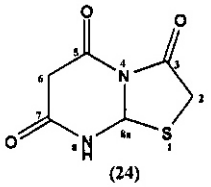


(11): R=H
(16):R=CH_3



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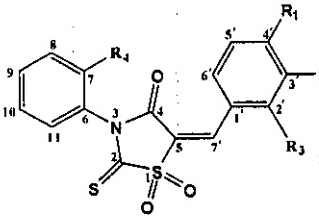
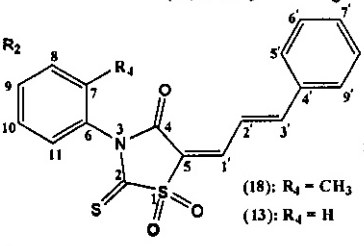
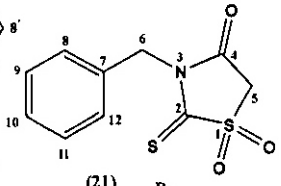




(12): R_1 = H, R_2 = H, R_3 = H, R_4 = H
(14): R_1 = H, R_2 = H, R_3 = OH, R_4 = H
(15): R_1 = OH, R_2 = OCH_3, R_3 = H, R_4 = H
(17): R_1 = H, R_2 = H, R_3 = H, R_4 = CH_3
(19): R_1 = H, R_2 = H, R_3 = OH, R_4 = CH_3
(20): R_1 = OH, R_2 = OCH_3, R_3 = H, R_4 = CH_3

(18): R_4 = CH_3
(13): R_4 = H



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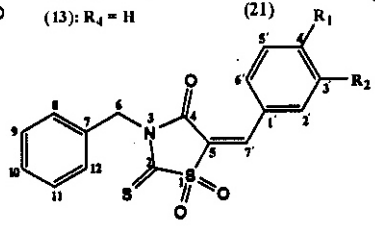
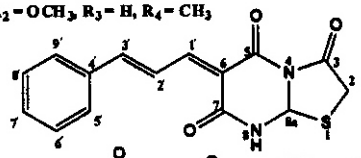


(23): R_1 = OH, R_2 = OCH_3
(22): R_1 = H, R_2 = H



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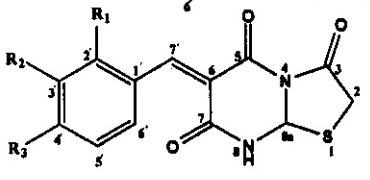
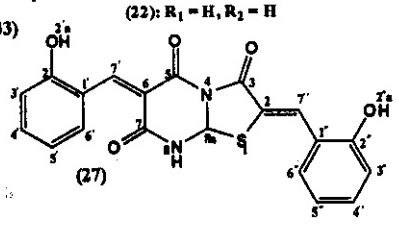


(25): R_1 = H, R_2 = H, R_3 = H
(26): R_1 = H, R_2 = H, R_3 = Cl
(28): R_1 = CH_3, R_2 = H, R_3 = H
(30): R_1 = H, R_2 = H, R_3 = OCH_3
(31): R_1 = H, R_2 = NH_2, R_3 = H



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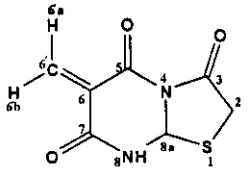

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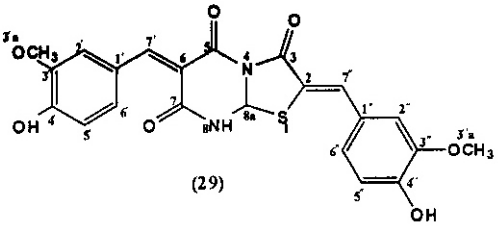

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