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In Vitro Antitumor Evaluation of Some New Tetra Substituted 1,2,4-Triazines

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SUMMARY. A new series of tetra substituted 1,2,4-triazines (**4**, **5**, **7** and **8**) was synthesized via the reaction of 3,1-oxazolinone (**1**) with thiosemicarbazide to give 6-hydroxy-5-(*p*-hydroxybenzylidene)-3-phenyl-2-(amino) thioxo-1,2,4-triazine (**3**). Treatment of 1,2,4-triazine derivative **3** with carbon disulphide and *p*-chlorophenacyl bromide yielded the corresponding 1,2,4-triazine derivatives **4** and **7**. Acetylation of tetra-substituted 1,2,4-triazines **4** and **7** with acetic anhydride gave tri acetyl and di acetyl derivatives **5** and **8**. Compounds structure was confirmed by IR, ^{1}H, ^{13}C-NMR, MS, and elemental analysis. The cytotoxic activities of some synthesized, 1,2,4-triazines were evaluated on human hepatocellular carcinoma cells (HepG-2) and human colon carcinoma cells (HCT-116) using the MTT method. We found that, compounds **5** (IC_{50} = 3.60 μg/mL) and **8** (IC_{50} = 4.40 μg/mL) have better activity against HCT-116 cell line than the reference doxorubcin (IC_{50} = 5.30 μg/mL), while compound **7** has best activity against HepG-2 cell line.

RESUMEN. Una nueva serie de 1,2,4-triazinas tetra-sustituidas (**4**, **5**, **7** y **8**) se sintetizaron mediante la reacción de 3,1-oxazolinona (**1**) con tiosemicarbazida para dar 6-hidroxi-5-(*p*-hidroxibencilideno)-3-fenil-2-(amino) tioxo-1,2,4-triazina (**3**). El tratamiento del derivado de 1,2,4-triazina 3 con disulfuro de carbono y bromuro de *p*-clorofenacilo produjo los correspondientes derivados de 1,2,4-triazina **4** y **7**. La acetilación de 1,2,4-triazinas tetra-sustituidas **4** y **7** con el anhídrido acético dio derivados de tri-acetilo y di-acetilo **5** y **8**. La estructura de los compuestos se confirmó por IR, ^{1}H, ^{13}C-NMR, MS y análisis elemental. Las actividades citotóxicas de algunas 1,2,4-triazinas sintetizadas se evaluaron en células de carcinoma hepatocelular humano (HepG-2) y células de carcinoma de colon humano (HCT-116) usando el método MTT. Encontramos que los compuestos 5 (IC_{50} = 3.60 μg/mL) y **8** (IC_{50} = 4.40 μg/mL) tienen mejor actividad contra la línea celular HCT-116 que la doxorrubicina de referencia (IC_{50} = 5.30 μg / mL), mientras que el compuesto **7** tiene mejor actividad contra la línea celular HepG-2.

KEY WORDS: HCT-116 cell line, HepG-2 cell line, synthesis, 1,2,4-triazine.

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