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Antiproliferative Activity of 3,5-Disubstituted Tetrahydro-2*H*-1,3,5-Thiadiazine Thione (THTT) Derivatives

Nuzhat Arshad[1]*, Irfanullah[2,3], Hamza Azam[1], Zahid Iqbal[1], Jamshed Hashim[2], Shumaila Jawaid[1], Muhammad Yaseen[3], Qurat-ul-Ain Hanif[1]

[1]*Department of Chemistry, NED University of Engineering. & Technology, Karachi, Pakistan*

[2]*H.E.J. Research Institute of Chemistry, International Center for Chemical and Biological Sciences, University of Karachi, Pakistan*

[3] *Institute of Chemical Sciences, University of Peshawar 25120, Pakistan*

**E-mail: nuzhat@neduet.edu.pk*

Introduction:

Cancer is the second major cause of deadly outcome in humans illnesses[1]. Currently chemotherapy have severe side effects and is challenging with present medications[2]. Thus, there is great demand of careful and effective chemotherapeutic agents. Among the therapeutic strategies, prodrug contribute more than one-third of the registered drugs today[3] that describe the low or inactive pharmalogical forms of active drug molecules. In reality, prodrug carry a mask on their active sites that open up/ unmask at the desired pharmaceutical targets under the optimal physiological conditions[4]. The prodrug are design to i) reduce activity towards unwanted pharmaceutical targets, ii) improve pharmacokinetics, and iii) reduce toxicity and side effects. In this context, Compound (1) have been reported as a prodrug of Zanamivir and Compound (**2**) as an antibacterial agent (Figure 1).

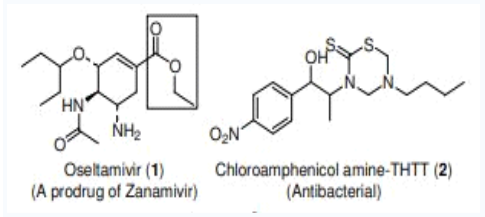
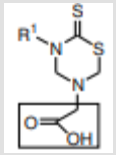
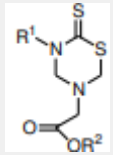
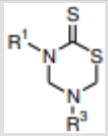
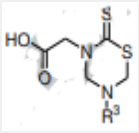


Figure 1. Biological Active Pharmacophores

Table 1.

S.No	Structure	PC3 (µM)	Hela (µM)	Standard (µM)
1.	 6 Examples	23.4-7.9 ± 3.1	23.8-2.4 ± 3.2	Doxorubicin (0.3)
2.	 4 Examples	N.A.-29.9 ± 0.3	N.A.-17.8 ± 5.1	Doxorubicin (0.3)
3.	 6 Examples	6.4-11.4 ± 2.7	3.2-4.0 ± 0.6	Doxorubicin (0.3)
4.	 4 Examples	N.A.	N.A.-21.8 ± 3.2	Doxorubicin (0.3)

Result s and Disscussions

In order to develop anticancer agents, we have prepared four different series of thiadiazine as shown in table-1 following our recent report[5] and evaluated for their anticancer potential against two cancerous cell lines. A moderate to significant potential is observed for both assays, we further evaluated these compounds cytotoxicity for 3T3 cell lines and their ability to transform into active drug by the action of enzyme.

Conclusion:

In conclusion, the developed compounds showed notable selectivity against Hella cell lines. Furthermore, these compounds especially, ester derivatives follow prodrug criterion of being nontoxic ,inactive and biotransormable in active form.

References:

1. Jemal, A., Siegel, R., Ward, E., Hao, Y., Xu, J., Murray, T. , Thun, M. J. Cancer statistics, CA, Cancer J. Clin. 2008, 58,71.
2. Szakacs, G., Paterson, J. K., Ludwig, J. A., Booth-Genthe, C., Gottesman, M. M. Nat Rev Drug Discov, 2006,5,219.
3. Stella, V. J. J. Pharm. Sci. 2010, 99, 4755.
4. Lesniewska-Kowiel, M. A.; Muszalska, I. Eur. J. Med. Chem. 2017, 129, 53; b) Huttunen, K. M.; Raunio, H.; Rautio, J. Pharmacol. Rev. 2011, 63, 750.
5. Arshad, N.; Hashim, J.; Ullah, I.; Minhas, M. A.; Aslam, J.; Ashraf, T.; Hamid, S. Z.; Iqbal, T.; Javed, S. Bioorg. & Med. Chem. Lett. 2018, 28, 3251.