SYNTHESIS, CHARACTERIZATION AND ANTIOXIDANE ACTIVITY OF N1-(5-CHLORO-2-OXOINDOLINE-3-YLIDENE) THIOCARBOHYDRAZONE SCHİFF BASES

1- Abstract.

In this study seven new Schiff bases were prepared from monothiocarbohydrazones and 5-chloro isatin. The monothiocarbohydrazones were synthesized in the presence of ethanol under reflux with the reaction thiocarbohydrazide and substituted aldehydes. The reaction of synthesized benzothiocarbohydrazone, 4-hydroxy benzothiocarbohydrazone, 3-ethoxy-4-hydroxyl benzothiocarbohydrazone, 3,5-dimethoxy-4-hydroxyl benzothiocarbohydrazone and 4-N, N, dimethly benzothiocarbohydrazone with 5-chloro isatin in acidic medium under reflux with N1- (5-Chloro-2-oxoindolin-3-ylidene) Shiff bases were obtained. The chemical structures of the products were confirmed by 1H-NMR, 13C-NMR, IR and elemental analysis. Physicochemical properties such as melting point, color and solubility were determined. In vitro antioxidant activity of all compounds was determined by 1,1-Diphenyl-2-Picril Hydrazil (DPPH) free radical scavenging method. Antioxidant activities of molecules and standard used Gallic Acid> 3,5-dimethoxy-4-hydroxyl benzothiocarbohydrazone> 3-ethoxy-4-hydroxyl benzothiocarbohydrazone> 4-hydroxy benzothiocarbohydrazone> Benzothiocarbohydrazone> N1- (5-Chloro-2-oxoindolin-3-ylidene) ) 4-N, N, dimethly benzothiocarbohydrazone> N1- (5-Chloro-2-oxoindolin-3-ylidene) 3, ethoxy-4-hydroxyl benzothiocarbohydrazone> 4-N, N, dimethly benzothiocarbohydrazone> N1- (5-Chloro-) 2-oxoindolin-3-ylidene) 3,5-dimethoxy-4-hydroxyl benzothiocarbohydrazone> N1- (5-Chloro-2-oxoindolin-3-ylidene) 4, hydroxy benzothiocarbohydrazone> N1- (5-Chloro-2-oxoindoline- 3-ylidene) benzothiocarbohydrazone.

Key Words**:** N1- (5-Chloro-2-Oxoindolin-3-Ylidene) Thiocarbohydrazone, Antioxidant Activity, DPPH method, NMR spectroscopy.

2- Devices and Chemicals Used.

5-chloro isatin, Thiocarbohydrazone and aldehydes are provided from Sigma-Aldrich Co. Ltd. LLC. company. Deionized purity water was used in each step. C, H and O elemental analyzes and FTIR analyzes were performed in Kastamonu University Central Research Laboratory. 1H-NMR and 13C-NMR analyzes were performed in Bolu Abant University Central Research Laboratory. All solvents were used in analytical purity. Absorbances were measured by SHIMADZU UVmini-1240 UV-Visible spectrophotometer (Schimadzu Corp., Kyoto, Japan manufactures) using a pair of equivalent quartz cuvettes of 1 cm thickness at 517 nm.

Compounds synthesized in the study were examined in two stages. In the first step, the synthesis of the semifinished products was performed and the synthesized compounds are given in Table 2.1. In the second step, the final products were synthesized and the synthesized compoundsaregiveninTable2.2.  
The chemical materials used in this study are as follows:

1) Thiocarbohydrazone

2) Benzaldehyde

3) 4, hydroxy benzaldhyde

4) 3,5 dimethoxy-4-hydroxyl –benzaldhyde

5) 3,ethoxy-4-hydroxyl –benzaldhyde

6) N1- 5-Chloro-2-oxoindolin-3-ylidene

7) 4-N,N, dimethly benzaldehyde

3- RESULTS AND DISCUSSION.

Some physicochemical parameters of the synthesized products are given in Table 3.1 for semi-products and Table 3.2 for final products. In addition to the structural determinations, the calculated and experimental elemental analyzes ((N), (C) and (H)%) of the compounds were performed and given in Table 3.3.

*Tablo 3.1.* Physicochemical Parameters of Synthesized Compounds (Semi-Product)

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Compound (Semi Product)** | **Molecular Weight** | **Melt Point (oC)** | **Colour** | **Resolution** | **Efficieny**  **(%)** |
| 1 | 194,27 | 184 | White | DMSO (+) | 74,73 |
| 2 | 210,27 | 214 | Light cream color | DMSO (+) | 74,84 |
| 3 | 254,32 | 206 | Light yellow | DMSO (+) | 76,73 |
| 4 | 270,32 | 226 | Light yellow- cream color | DMSO (+) | 79,61 |
| 5 | 237,34 | 198 | % 70 yellow- % 30 green | DMSO (+) | - |

*Tablo 3.2* Physicochemical Parameters of Synthesized Compounds (Final Product)

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Compound (Final Product)** | **Molecular Weight** | **Melt Point (oC)** | **Colour** | **Resolution** | **Efficieny**  **(%)** |
| 1 | 357,85 | 234 | % 80 Light brown- % 20 Yellow | DMSO (+) | 56,70 |
| 2 | 373,85 | 254 | Light orange | DMSO (+) | 82,96 |
| 3 | 417,90 | 248 | Matte yellow | DMSO (+) | 76,44 |
| 4 | 433,90 | 267 | % 30 Brown-% 10 orange-% 60yellow | DMSO (+) | 90,54 |
| 5 | 400,92 | 238 | Dark brown | DMSO (+) | 50,29 |

*Tablo 3.3.*Calculated and experimental elemental analysis of synthesized compounds

((N),(C) ve (H)%)

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Compound** | **Calculated** | | | **Experimental** | | |
| **%N** | **%C** | **%H** | **(N) %** | **(C) %** | **(H) %** |
| Son Ürünler 1 | 19,561 | 53,653 | 3,380 | 18,998 | 52,769 | 3,219 |
| Son Ürünler 2 | 18,724 | 51,357 | 3,235 | 18,312 | 50,829 | 3,193 |
| Son Ürünler 3 | 16,750 | 51,687 | 3,859 | 16,374 | 50,730 | 3,813 |
| Son Ürünler 4 | 16,132 | 49,781 | 3,716 | 15,897 | 48,153 | 3,676 |
| Son Ürünler 5 | 20,951 | 53,876 | 4,274 | 20,615 | 51,973 | 4,236 |
| \*YarıÜrünler 1 | 28,825 | 49,415 | 5,188 | - | - | - |
| \*YarıÜrünler 2 | 26,632 | 45,655 | 4,793 | - | - | - |
| YarıÜrünler 3 | 22,019 | 47,184 | 5,548 | 21,387 | 46,417 | 5,447 |
| YarıÜrünler 4 | 20,716 | 44,391 | 5,220 | 20,375 | 42,926 | 5,131 |
| \*YarıÜrünler 5 | 29,49355 | 50,560 | 6,370 | - | - | - |

\*These compounds have been synthesized previously and are available in the literature.

4- CONCLUSİON

Isatin and its derivatives, which are known to exhibit many biological activities in the pharmaceutical field, constitute an important class of hetero-compounds. In this study, Schiff base compounds with azomethine group (-C = N–) bound to different aldehydes synthesized as intermediates and final product compounds formed with 5-chloro isatin were investigated in terms of antioxidant activities. It has been found that the antioxidant activities of the semi products are obtained not only from the substitutes present on the aromatic ring, but also from the H donor groups bound to the azomethine group and therefore show higher activity than the end products containing isatin. Although all synthesized molecules exhibit lower activity than gallic acid, which is a natural antioxidant, intermediates with methoxy and ethoxy groups can be considered as an alternative industrial product after toxicological and biological studies.

5- References

[1] URL-1. <https://en.wikipedia.org/wiki/Schiff_base>

[2] [IUPAC](https://en.wikipedia.org/wiki/International_Union_of_Pure_and_Applied_Chemistry), [Compendium of Chemical Terminology](https://en.wikipedia.org/wiki/Compendium_of_Chemical_Terminology), 2nd ed. (the "Gold Book") (1997). Online corrected version:  (2006–) "Schiff base".

[3]"604211HYPERLINK "%22http://pubs.rsc.org/en/Content/ArticleLanding/HYPERLINK%203-------------\*\*ghjhgj Chohan ZH, Hernandes MZ, Sensato FR, et al. Sulfonamide–metalcomplexes endowed with potent anti-Trypanosoma cruzi activity. JEnzyme Inhib Med Chem. 2014;29(2):230–236.6.

[4] Eroglu E. Some QSAR studies for a group of sulfonamide Schiff base ascarbonic anhydrase CA II inhibitors. Int J Mol Sci. 2008;9(2):181–197

[5] Eman T., S.(2016).Preparation and Characterization of new Schiff base Derived from Pyridineand its metal complexes.Int. J. Curr. Res. Chem. Pharm. Sci. 3(4):118-123.

[6] Abu-Khadra, A. S., Farag, R. S., & Abdel-Hady, A. E. D. M. (2016). Synthesis, characterization and antimicrobial activity of Schiff base (E)-N-(4-(2-hydroxybenzylideneamino) phenylsulfonyl) acetamide metal complexes. *American Journal of Analytical Chemistry*, *7*(3).

[7] URL-2. https://shodhganga.inflibnet.ac.in/bitstream/10603/8812/6/06\_chapter%

201.pdf

[8] Da Silva CM, Da Silva DL, Modolo LV, Rosemeire B Alves, Maria A de Resende, et al. (2011) Schiff bases: A short review of their antimicrobial activities. J of adv res 2(1): 1-8.

[9] Hodnett, E. M., & Dunn, W. J. (1970). Structure-antitumor activity correlation of some Schiff bases.*Journal of Medicinal Chemistry*, *13*(4), 768-770.

[10] Hodnett, E. M., & Mooney, P. D. (1970). Antitumor activities of some Schiff bases. *Journal of medicinal chemistry*, *13*(4), 786-786.

[11] Urbach, F. L. (1981). *The properties of binuclear copper centers in model and natural compounds*(Vol. 13, p. 73). Dekker: New York.

[12] Patai S Ed., "The Chemistry of the Carbon-Nitrogen Double Bond", J. Wiley & Sons, 1970, London.

[13] Jungreis E and Thabet S, "Analytical Applications of Schiff bases", Marcell Dekker, 1969, New York

[14]S.Gaur, Assian J. Chem. 15(1), 250 (2003). (b) M.J.Gemi, C.Biles, B.J.Keiser, S.M.Poppe, S.M. Swaney, W.G.Tarapley, D.L.Romeso, Y.Yage, J.Med.Chem. 43(5), 1034 (2000)..

[15]Tisato, F., Refosco, F., & Bandoli, G. (1994). Structural survey of technetium complexes. *Coordination Chemistry Reviews*, *135*, 325-397.

[16]Balsells, J., Mejorado, L., Phillips, M., Ortega, F., Aguirre, G., Somanathan, R., & Walsh, P. J. (1998). Synthesis of chiral sulfonamide/Schiff base ligands. *Tetrahedron: Asymmetry*, *9*(23), 4135-4142.

[17] Isloor, A. M., Kalluraya, B., & Shetty, P. (2009). Regioselective reaction: synthesis, characterization and pharmacological studies of some new Mannich bases derived from 1, 2, 4-triazoles. *European journal of medicinal chemistry*, *44*(9), 3784-3787.

[18] Krishnaraj, S., Muthukumar, M., Viswanathamurthi, P., & Sivakumar, S. (2008). Studies on ruthenium (II) Schiff base complexes as catalysts for transfer hydrogenation reactions. *Transition Metal Chemistry*, *33*(5), 643.