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Preparation, Diagnosis and Evaluation of Cyclic-Tryptophan Derivatives as Anti Breast cancer Agents

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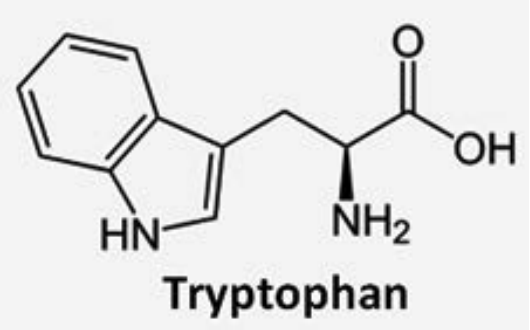
The importance of research lies in the treatment of cancerous tumors due to the spread of cancerous tumors in recent decades, so researchers have to insist on finding alternative and more treatments safe from chemotherapy and radiation, which are derivatives of some amino acids, which we attended in our current research. Also, some research showed that taking tryptophan for 3 days before exercise can improve energy and efficiency during exercise, but other preliminary research shows that taking tryptophan during exercise does not improve endurance during cycling exercises. For a few days before exercise to notice any benefit. In this research, we prepared derivatives of cyclic tryptophan and studied their efficacy as anti-tumors, and they gave good results in reducing the size of cancerous tumors and reducing their spread in the body., then sympathy all synthesized new cyclic-tryptophan compounds by numerous techniques (FT.IR ,H.NMR)–spectrophotometric, other physical and chemical properties ,with studying for one of new prepared derivatives as anti breast cancer.

Keywords: Anti Breast; Anticancer; Heterocyclic; Tryptophan; Triazole.

In 1901, Frederick Hopkins was able to isolate tryptophan for the first time. Hopkins extracted tryptophan from hydrolyzed casein, successfully extracting (4-8 g) of tryptophan from (600 g) of crude casein[1,2]. Tryptophan is a less common amino acid in proteins, but it plays an important structural or functional roles wherever it is found. For example, the residues tryptophan and tyrosine play special roles in 'fixing' membrane proteins within the cell membrane. In addition, the functions of tryptophan include being a vital precursor to compounds[3-5], Tryptophan stimulates serotonin levels in the brain, which can treat depression and anxiety. Therefore, you can take tryptophan supplements to reduce these indications[6-8]. Tryptophan helps increase growth hormones, so it is essential for the proper growth of children and infants. Tryptophan is used to treat insomnia, due to the presence of serotonin, which is useful for controlling sleep patterns[9-11]. People who suffer from migraines are advised to take doses of tryptophan regularly, and to eat foods rich in tryptophan, which also helps prevent anxiety attacks, which improves a person's reactions. It works to reduce appetite for food, because serotonin helps to make you feel satiated and reduce food intake. Thus, losing weight helps reduce diabetes and problems related to cardiovascular disease[12-14]. The body needs tryptophan to produce niacin, which helps generate good cholesterol and lower bad cholesterol. Foods rich in tryptophan also help convert carbohydrates into energy and

maintain a healthy digestive system, skin, hair and eyes[15-17], After we absorb tryptophan from food, our bodies convert it into 5-hydroxytryptophan, an amino acid that works in the brain and central nervous system by increasing the production of the chemical serotonin, and after our bodies convert it to this amino acid[18-22], it then turns into serotonin, melatonin[23-27] and Vitamin B6 (nicotinamide).

Some studies claim that tryptophan supplements may be effective as a sleep treatment and antidepressant. These findings are associated with its role in the synthesis of serotonin and melatonin[28-30]. Excessive encouragement of serotonin on postsynaptic (5-HT1A and 5-HT2A) receptors at the central and peripheral levels can have negative consequences for the organism[31-34]. This is known as serotonin syndrome and can be fatal. Although this syndrome can be caused by taking medications (eg, Prozac) or using drugs (eg, LSD, MDMA, methylphenidate, bath salts...), it is not likely to be caused by the consumption of nutritional supplements[35-39].



Scheme 1. Trytophan

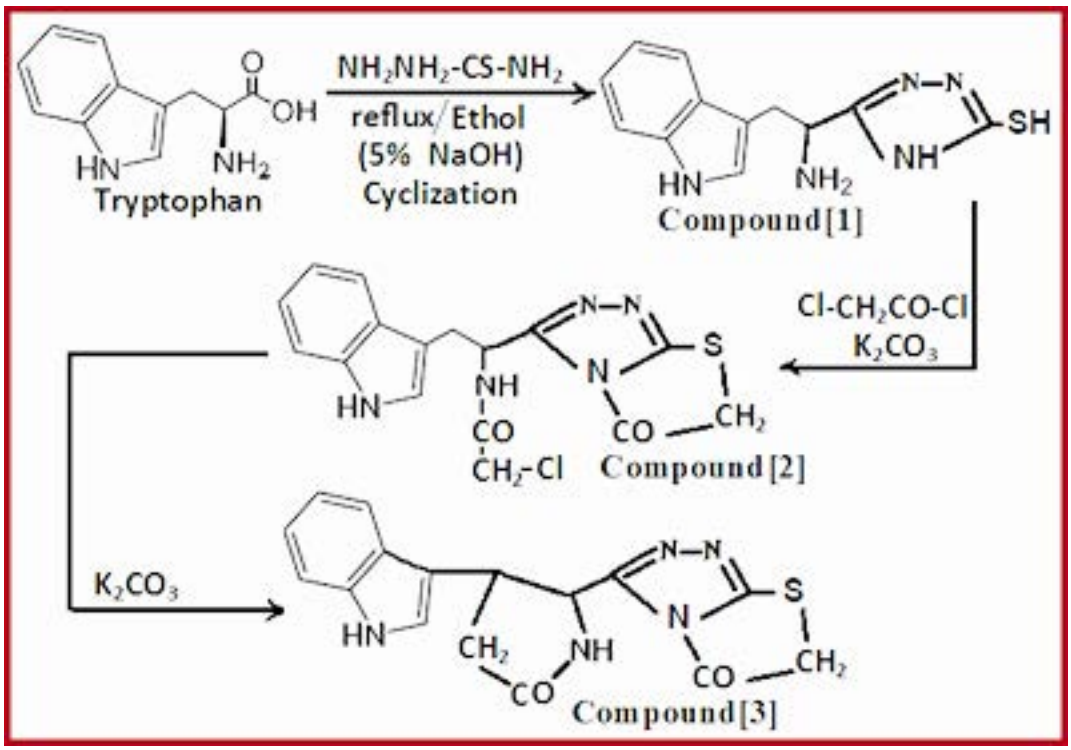
Experimental Part

Because of the importance of the prepared compounds in this research that they were studied as anti-cancer agents, we were keen to provide materials with high purity and from international companies with high technology in the production of chemicals. Also, the measurements were made on the following devices represented by ((FT-IR spectra (FT-IR 8300 Shimadzu) in the range (400-4000) cm^{-1} with KBr-discs., ^{1}H.NMR–Spectra with (DMSO)–solvent .,besides to anti breast cancer studies.

Synthesis Progressions [8-12]

Preparation Path of Compound{1}

Compound {1} formatted by reaction of tryptophan (0.01 mole) with thiosemicarbazide



Scheme 2. Synthesis of Compounds{1 ,2 ,3}

(0.01 mole) in presence of (5% of NaOH) with mechanical rotation for (16 hrs) in absolute ethanol permitting to mentioned methods[8-12] to produce precipitation that acts compound{1},the last step ,filtered ,dried ,then recrystallized to give pure compound.

Preparation Path of Compound{2}

Compound {2} formatted by reaction of compound{1} (0.01 mole) with chloroacetoyl chloride (0.02 mole) in presence of (K_2CO_3) with mechanical rotation for (4 hrs) permitting to methods[8-12] to yield precipitation that acts compound{2},the last step ,filtered ,dried ,then recrystallized to give pure compound.

Preparation Path of Compound{3}

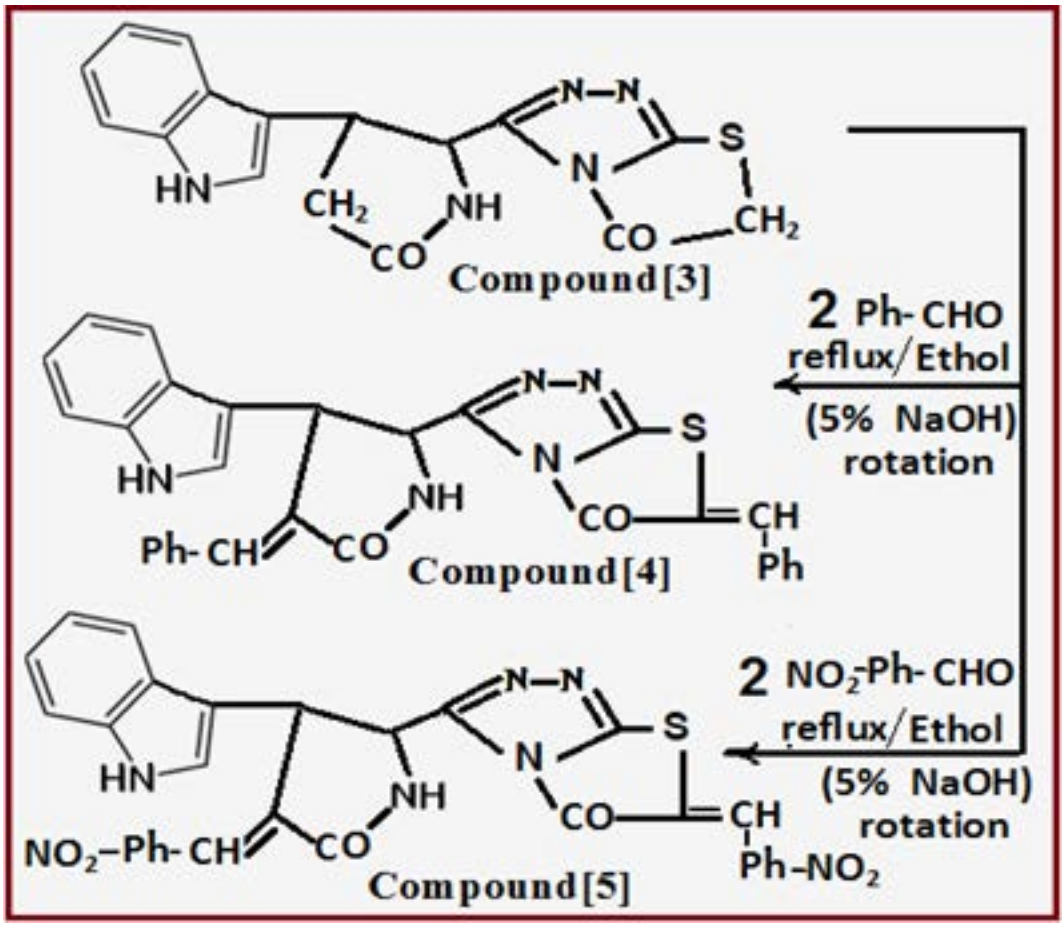
Compound {3}cyclized by cyclization reaction of compound{2} (0.01 mole) with in presence of (K_2CO_3) with mechanical rotation and reflux for (6 hrs) permitting to methods[8-12] to yield precipitation that acts compound{3},the last step ,filtered ,dried ,then recrystallized to give pure compound.

Preparation Path of Compound{4}

Compound {4} formatted by reaction of compound {3} (0.01 mole) with benzaldehyde (0.01 mole) in presence of (5% of NaOH) with mechanical rotation for (12 hrs) in absolute ethanol permitting to mentioned methods[8-12] to produce precipitation that acts compound{4},the last step, filtered ,dried ,then recrystallized to give pure compound.

Preparation Path of Compound{5}

Compound{5} formatted by reaction of compound{3} (0.01 mole) with m-nitrobenzaldehyde (0.01 mole) in presence of (5% of NaOH) with mechanical rotation for (13 hrs) in absolute ethanol permitting to mentioned methods[8-12] to produce precipitation that acts



Scheme 3. Synthesis of Compounds{4 , 5}

compound{5},the last step ,filtered ,dried ,then recrystallized to give pure compound.

RESULTS AND DISCUSSION

The prepared tryptophan-derivatives have been premeditated by different chemical performances and studies against cancerous cells:

Spectral Evidences of prepared Compounds

FT.IR- Investigation of Manufactured Derivatives: The bands of important groups in spectra provided strong evidences for new synthesized compound via disappearance of bands and appearance other new bands that point to formation of the new derivatives that represented by :

Compound {1}: appearance bands at (3282 , 3300)Cm^{-1} due to (NH_2) of amine group, band at (3223)Cm^{-1} due to (NH) of amine group in triazole cycle, also at (2445)Cm^{-1} due to (SH) of thiol group, band at (1652)Cm^{-1} due to (C=N) of endocycle of triazole, at (2978)Cm^{-1} caused by (CH) aliphatic permitting to literature [16] .

Compound {2}: appearance band at (3369)Cm^{-1} due to (NH) of amine group in tryptophan, band at (1184)Cm^{-1} due to (S-CH_2) of sulfide group, also at (1664)Cm^{-1} caused by (C=N) of endocycle of triazole, band at (2918)Cm^{-1} by reason of (CH) aliphatic, at (792)Cm^{-1} as a result of (C-Cl), band at (1681)Cm^{-1} due to (C-CO) amide group.

Compound {3}: appearance band at (3421)Cm^{-1} caused by (NH) of amine group in tryptophan, band at (1180)Cm^{-1} due to (S-CH_2) of sulfide group, band at (1643)Cm^{-1} down to (C=N) of endocycle of triazole, band at (2954)Cm^{-1} due to (CH) aliphatic, band at (1664)Cm^{-1} down to (C-CO) amide group.

Compound {4}: appearance band at (3355)Cm^{-1} by reason of (NH) of amine group in tryptophan, band at (1148)Cm^{-1} due to (S-CH_2) of sulfide group, band at (1655)Cm^{-1} due to (C=N) of endocycle of triazole, band at (2919)Cm^{-1} due to (CH) aliphatic, band at (1679)Cm^{-1} due to (C-CO) amide group, band at (3092)Cm^{-1} due to (CH=C) alkene , according to literature [16].

Compound {5}: appearance band at (3310)Cm^{-1} by reason of (NH) of amine group in tryptophan, band at (1133)Cm^{-1} down to (S-CH_2) of sulfide group, at (1647)Cm^{-1} due to (C=N) of endocycle of triazole, band at (2906)Cm^{-1} down to (CH) aliphatic, band at (1682)Cm^{-1} down to (C-CO) amide group, band at (3097)Cm^{-1} down to (CH=C) alkene, bands at (1327 , 1511)Cm^{-1} due to (NO_2)

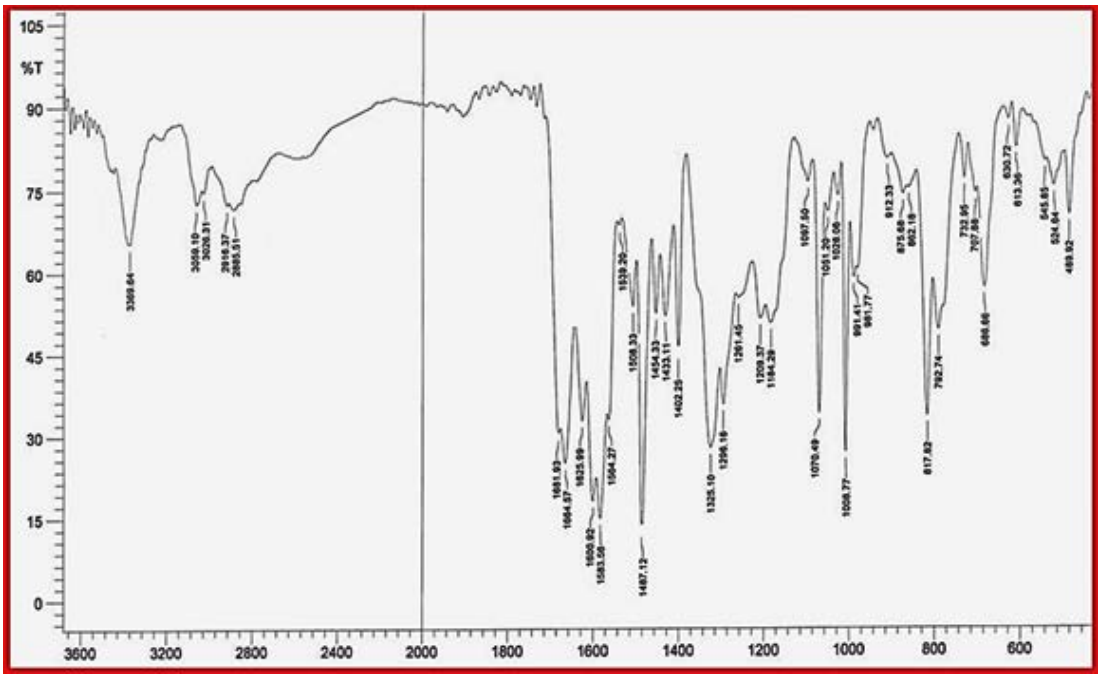


Fig. 1. I.R Spectrum of The formatted Compound {2}

nitro group., Other frequencies appeared in some figures (1 , 2) .

[1]H.NMR- Investigation of Manufactured Derivatives: The signals of important groups in spectra provided strong evidences for new synthesized compound via disappearance of peaks and appearance other new peaks that point to formation of the new derivatives that represented by : signals at (4.55 to 5.00) due to proton of amine group (NH) ,signals at (10. 12 to 10. 80) due to proton of amide (-NH-CO), signals at (6. 60-7. 95) due to protons of phenyl ring in compounds {2 ,3 , 4, 5}respectively, signal at (3.05) due to proton of (CO-CH_2-S) in compounds {2 ,3}respectively , signal at (4.45) due to proton of (CH=C) of alkene in compounds {4 ,5}respectively permitting to literature [16] .,Some peaks in some figures (3, 4).

Some physical and Chemical characterization

All other physical and chemical analysis besides to some description in Table (1):

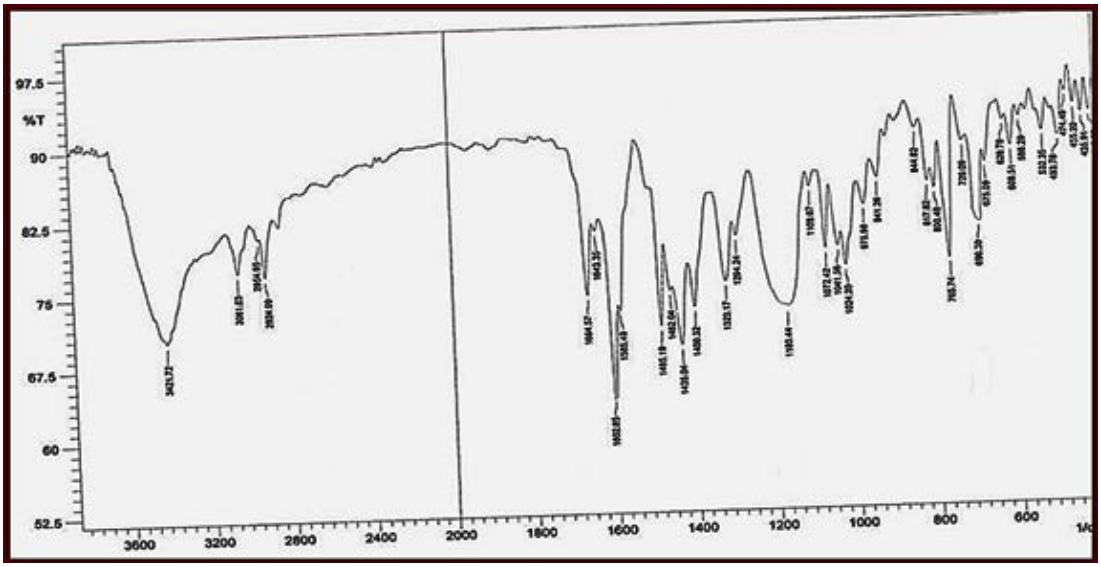


Fig. 2. I.R -Spectrum of The formatted Compound {3}

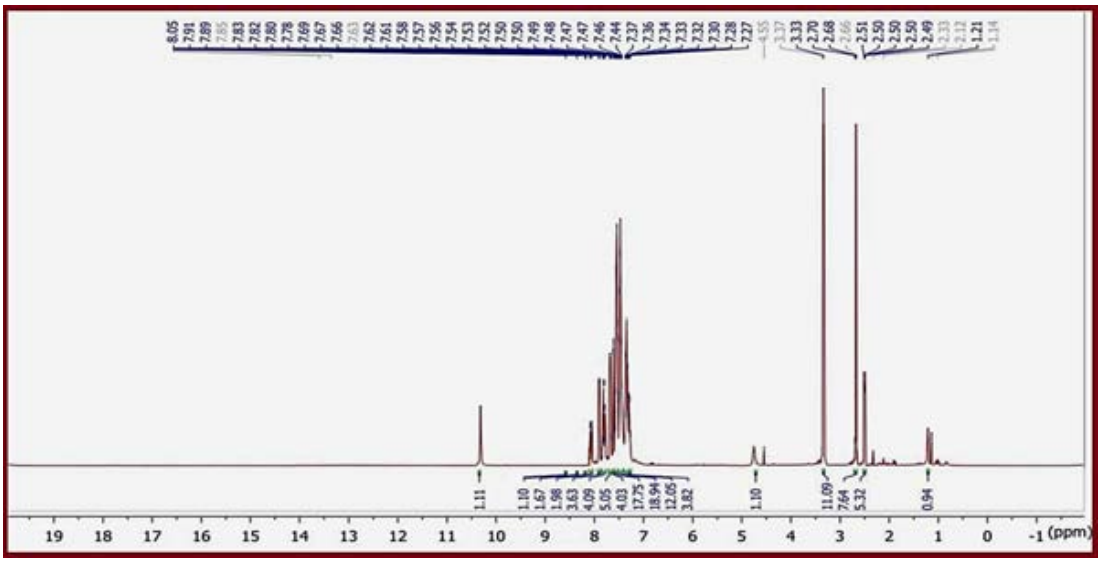


Fig. 3. H.NMR-Spectrum of Compound{2}

Table 1. Some Physical Properties of New Compounds

Comps	Product %	Color	M .P (C °)	Rf	Solvents (TLC)
{ 1 }	82	Orange	160	0.64	Ethanol : Hexane
{ 2 }	78	Yellowish orange	182	0.68	Ethanol : Hexane
{ 3 }	70	Deep Yellow	194	0.64	Ethanol : Hexane
{ 4 }	82	Yellowish Red	200	0.58	Ethanol : Hexane
{ 5 }	80	Bill Orange	216	0.60	Ethanol : Hexane

Table 2. Mean Percentage (%) for each cell line (Respond to Treatment) for Derivative{2}

Concentration of Tryptophan-Derivative [2] / (μ g/Ml^{-1})	MCF-7		WRL	
	Mean	SD	Mean	SD
400	50.00	1.34	49.44	1.14
200	63.11	2.21	27.10	0.65
100	74.12	5.32	26.41	2.06
50	80.13	4.12	19.03	0.92
25	89.91	0.87	10.08	1.58
12.5	90.80	0.88	9.34	2.44
6.25	91.24	0.22	9.04	1.16

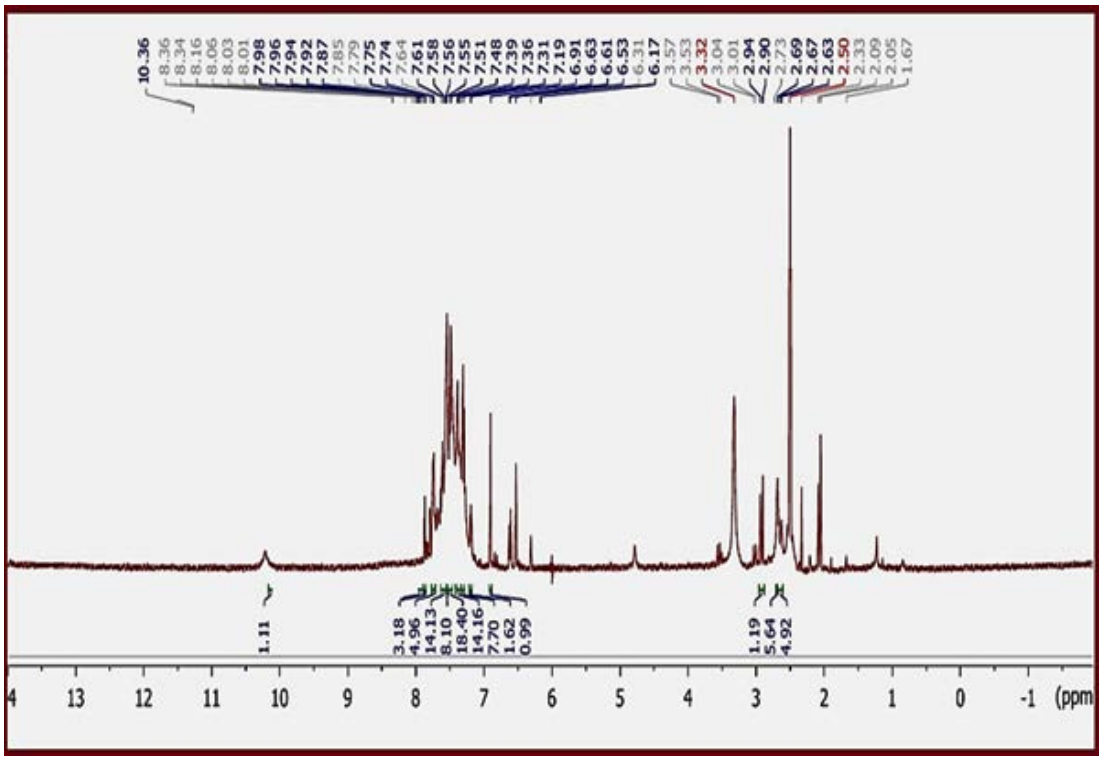


Fig. 4. H.NMR-Spectrum of Compound{4}

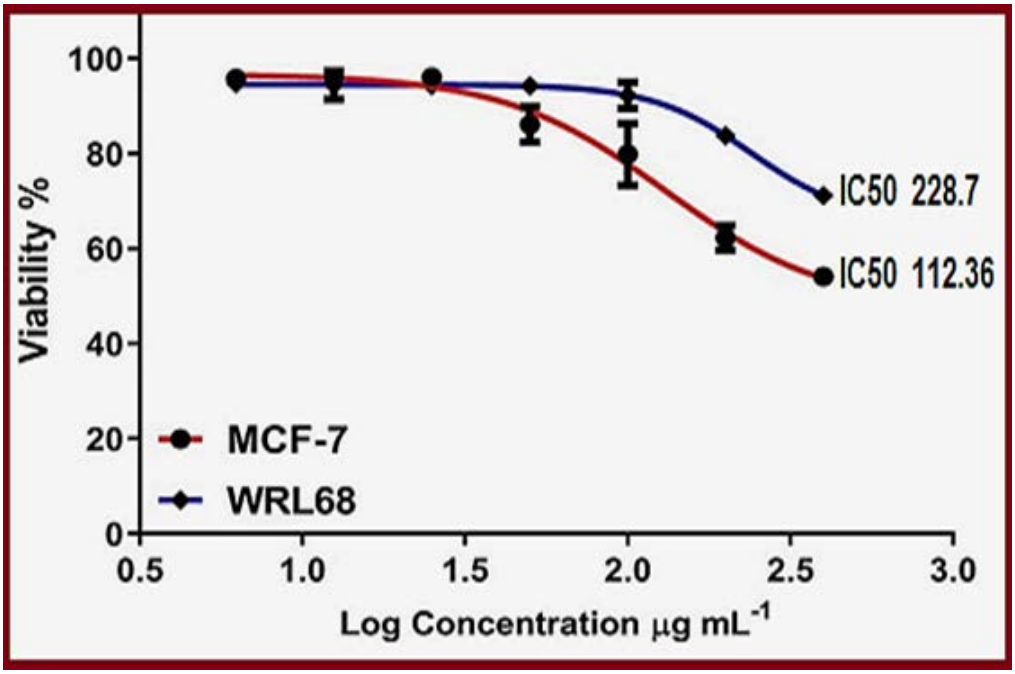


Fig. 5. Effect of Tryptophan-Derivative [2] on Breast Cancer Cells

Analysis of derivatives with Breast Cancer

The study was conducted to test the effectiveness of medicinal derivatives through the methods listed in the references[17, 18] .

CONCLUSION

The manufactured of Tryptophan-Derivative[2] gave multiple strong evidences about structures of compounds were stable, and all Tryptophan-Derivatives have high solubility in ethanol , DMSO, Methanol and other solvents. And have good activity against breast breast cancer cells.

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Ethical clearance

Ethics committee refer that there is no plagiarism and there is no mistakes or wrong results in this work.

Conflict of interest

The authors declare that there is no conflict of interest.

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