

# The Lipid Solubility of Most Drugs Play Important Role of Its Pharmacological Action and Duration of Action



Rezk R Ayyad<sup>1</sup>, Ahmed M Nejm<sup>1</sup>, Yasser Abdel allem Hassan and Ahmed R Ayyad<sup>3</sup>

<sup>1</sup>Pharmaceutical Medicinal Chemistry Department, Faculty of Pharmacy, ALAZHAR University, Cairo, Egypt

<sup>2</sup>Pharmaceutics and Pharmaceutical Technology Department, Faculty of Pharmacy, Delta University for Science and Technology, Gamasa, Addaqahly, Egypt

<sup>3</sup>Faculty of Medicine, Asfendiyarov, Kazakh, National Medical University (KazNMU)

**Submission:** September 04, 2023; **Published:** October 02, 2023

**\*Corresponding author:** Rezk R Ayyad, Pharmaceutical Medicinal Chemistry Department, Faculty of Pharmacy, ALAZHAR University, Cairo, Egypt

## Abstract

The fact of human body and animal body formed of organs which formed of tissue which its constituents is the cells. The cell enveloped by cell membrane which contain more its content of lipid compounds to protect the cell. Hence when the chemical compounds (drugs) across to the cytoplasm of the cell must has a lipophilic character. Also, there is a fact the oily substances do not mix with the watery substance, so must be take a cream form (water in oil or oil in water emulsion), so the drugs must be soluble in lipid to across the cell to obtain the desirable effect. The partition co-efficient is a significant expression of lipid solubility.

Many of drugs convert to prodrug this prodrug has highly lipid solubility and has long duration of action e.g. testosterone cybionate, rolitetracycline, penicillin procaine, benzylpenicillin, nandrolone decanoate...etc., on the other hand the water soluble compounds (hydrophilic drugs) e.g. vitamin B complexes which exert its effects and excreted from the kidney quickly this indicate to no long duration of vitamin B complex except the cyanocobalamin (vit.B12) which incorporated to sesame oil to depote in the body to treatment the inflammation of nerves of diabetic patients which suffering from neuropathy.

**Keywords:** Lipid Solubility; Hydrophilic Drugs; Partition Co-Efficient; Prodrugs; Duration of Action; Pharmacological Action; Blood Brain Barrier (BBB)

## Introduction

In the first when the chemist design new drug, or the physician want to describe some drugs in some diseases must be taken in his mind the lipid solubility of the drug to sure reach the drug to target site and may be prolonged its action. The partition co-efficient is significant for lipid solubility in vitro where represented by the solubility of the drug in n-octane (represent the lipid phase), the water which represent the aqueous phase, if the chemical compound (drug) soluble in octane phase will be soluble in lipid and if soluble in water will be water soluble. The partition co-efficient is the ratio of drug soluble in n-octane to water. Many of drugs may be react with organic acids (acetic, propionic, buteric, pentanoic, hexanoic, heptanoic, octanoic, nonanoic, decanoic, undecanoic, dodecanoic) or fatty acids (saturated non-essential, non-saturated essential), to make esters, these esters don't water soluble (many of esters mainly water insoluble), so these esters

lipid soluble not only this fat but the drugs become prodrugs [1-10]. The lipid solubility of drug esters make the drugs reach to the target sites due to lipid solubility across the cell membrane of (cell, tissue, or organ), furthermore the drug esters easily hydrolyzed by esterase enzyme in the body. Hence the pharmacists, physicians, and the pharmaceutical companies must take in consideration the lipid solubility in your works to reach the maximum activity of the drugs [11-15].

## Chemistry and Discussion

The drugs which are water soluble not stay in the body for long time e.g., water soluble vitamins where it excreted from the kidney [16]. Vit.B1 (Thiamine) [Figure 1]. Thiamine is important to growth and vital functions and present in many foods as (dicots) and is important for metabolism of carbohydrates, lipids, and protein, decrease of the thiamine in the body will cause

dysfunction on the body and lead to Beri Beri disease, so we must take in consideration the solubility of thiamine and its excretion quickly from the kidney [17-20].

The Riboflavin is vit.B2 which is essential for the functions of

the body [Figure 2] Riboflavin plays many important roles in vital processes in the body, the very important role is in carbohydrates (glucose) metabolism which enter the structure of FAD, which is Co-enzyme to enzymes which act on glucose, also water soluble and excreted from the kidney [21-23].

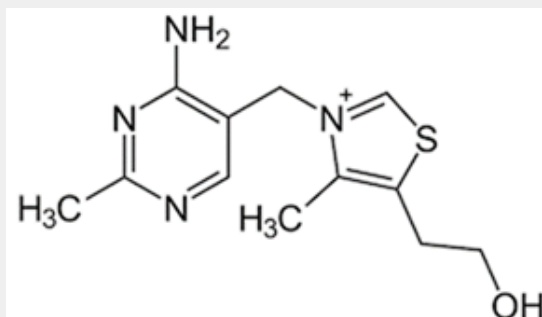


Figure 1.

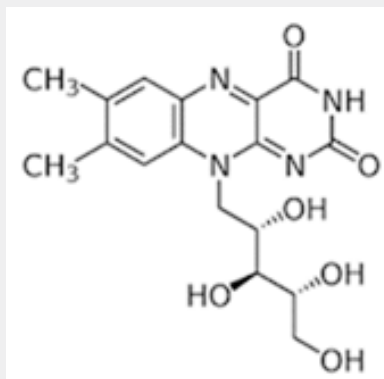


Figure 2.

Nicotinamide is vit.B3 one of the vit.B complex group which make vital role in skin health and its Important role enter the structure NAD and NADP which are important as co-enzymes to the enzyme which act on glucose, so when decreased in the body due to its water solubility and excreted from kidney may be increase the glucose level in the body [Figure 3] [24-25].

Pyridoxine is a vit.B6 and is also member of vit.B complex which is important for keep on the health nerves especially in diabetic patients which after time of chronicity wine neuropathy, also used in pregnant woman emesis (also has water solubility and excreted from the body via excretion routes) [Figure 4] [26-30].

Vit.B12 (cyanocobalamin) also one of the vit.B complex which soluble in water and decrease in the body, so it must be taken more times for diabetic and pre diabetic patients because it keep and treat the inflammation of nerves caused by high level of glucose in the blood. As we mentioned above, the cyanocobalamin in sesame oil prolonged in the body [Figure 5] [31-35].

Vit.C (Ascorbic acid) is a water soluble vitamin plays an essential role in the body to maintain a healthy life as it act as powerful antioxidant, raised the immune level so enhance immunity against infection and help in relief the symptoms of common cold and other viral infections, also it enhance absorption of Ca so maintain a healthy bone, also ascorbic acid (Vit.C) water soluble and excreted from the body and the body need take repeated administration to keep its function in body [Figure 7], all the mentioned vitamins are essential for human, but its water solubility make them make them around disadvantage [36-40].

Also, Pantothenic acid (vit.B5), Biotin (vit.B7), Folic acid (vit. B9) and Amygdaline (vit.B17 which is used as anticancer) these compounds are water soluble and has low concentration in the body [Figure 8-10]. N.B. The vitamins which are soluble in water must be alarmed to physicians of diabetes and must calculate the actual need of vitamin B complexes, which are very important in diabetic treatment [41-45].

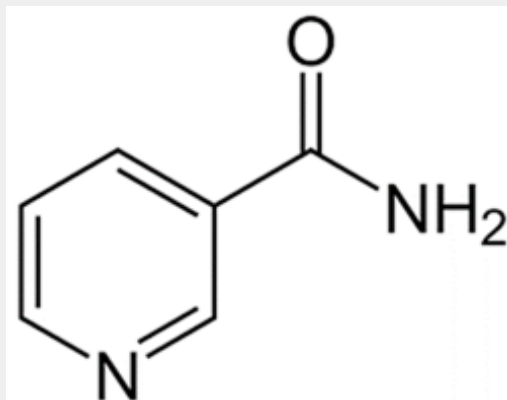


Figure 3.

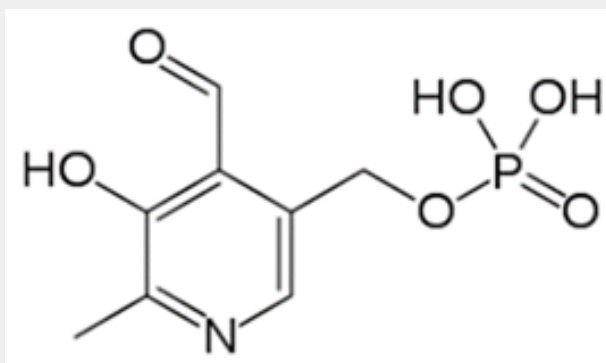


Figure 4.

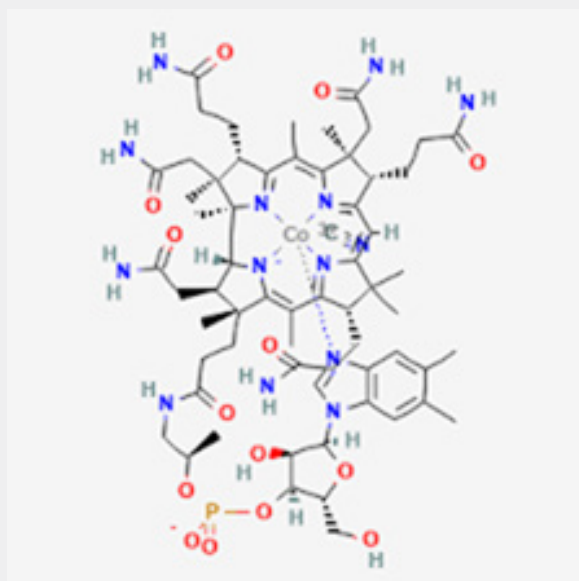


Figure 5.

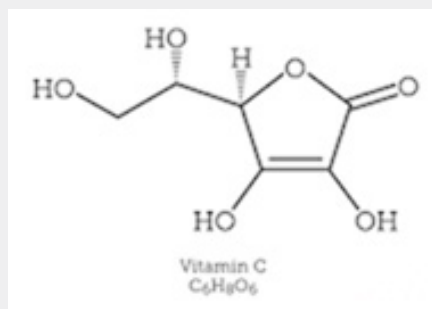


Figure 6.

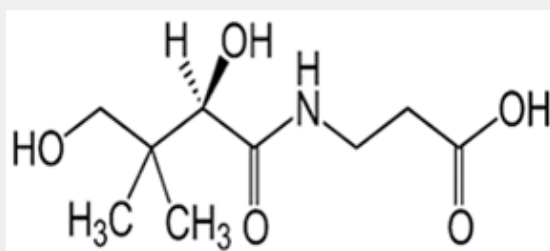


Figure 7.

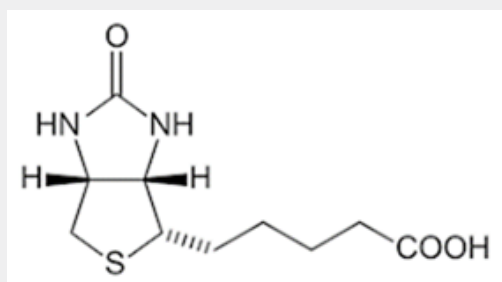


Figure 8.

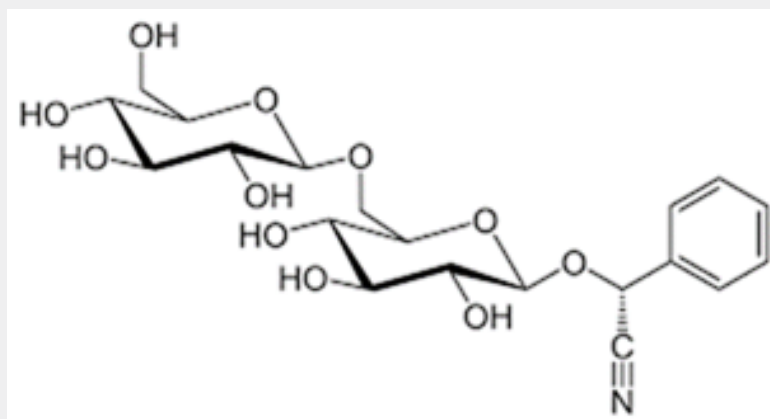


Figure 9.

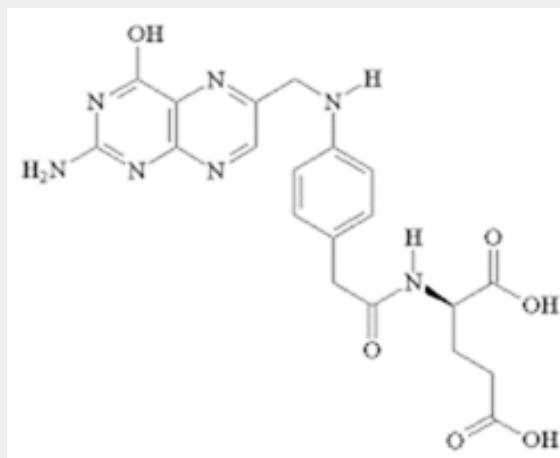


Figure 10.

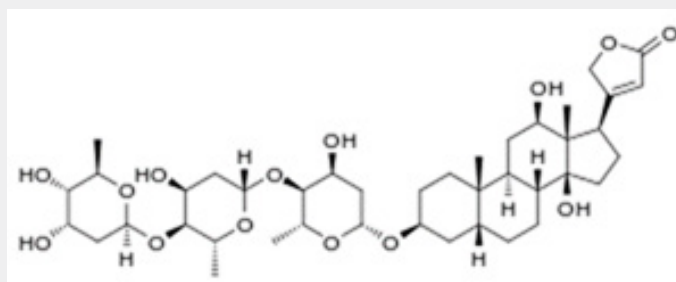


Figure 11.

## Conclusion

The lipid solubility must be taken in consideration in many drugs when we want design a new drug or the physician want to describe a drug to patient. Absolutely not all drugs are highly lipid solubility due to the accumulation property e.g., [Figure 11] Digoxin not merely, some compounds if stored in the body may be harm to it (toxicity of digoxin) or cause disease (edema of mineralocorticoids hormone), in spite we attention to the importance of lipid solubility of the drugs to sure reach it to the target sites or to give prolonged action.

## References

1. RR Ayyad, AM Nejm, AR Ayyad (2023) The Isomers of Some Drugs One Effective and the Other Is Toxic or Ineffective Current Research in Medical Sciences 2(2): 58-62.
2. RR Ayyad, AM Nejm, AR Ayyad (2023) The Activity of Some Antibiotics Depend on Stereochemistry of Them (Its Structure) Journal of Progress in Engineering and Physical Science 2(2): 5-7.
3. H Mahdy, M Shaat, R Ayyad (2022) Recent Advances in Drugs Targeting Protein Kinases for Cancer Therapy. Al-Azhar Journal of Pharmaceutical Sciences 66(2): 56-86.
4. A Ibrahim, HM Sakr, RR Ayyad, MM Khalifa (2022) Design, Synthesis, In-Vivo Anti-Diabetic Activity, In-Vitro  $\alpha$ -Glucosidase Inhibitory Activity and Molecular Docking Studies of Some Quinazolinone Derivatives Chemistry Select 7(14): e202104590.
5. R Ayyad, H Sakr, A Gaafer (2022) Design and Synthesis of New Compounds Derived from Phenyl Hydrazine and Different Aldehydes as Anticancer Agents International Journal of Organic Chemistry 12 (1): 28-39.
6. IA Osman, RR Ayyad, HA Mahdy (2022) New pyrimidine-5-carbonitrile derivatives as EGFR inhibitors with anticancer and apoptotic activities: design, molecular modeling, and synthesis New Journal of Chemistry 46 (24): 11812-11827.
7. RR Ayyad, AM Nejm, YH Abdelaleem, AR Ayyad (2023) Hydrophobicity, Transport and Target Sites of Action Are Important for the Activity of Many Drugs Current Research in Medical Sciences 2(3): 15-19.
8. M Al Ward, AE Abdallah, M Zayed, R Ayyad, M El-Zahabi (2023) New immunomodulatory anticancer quinazolinone based thalidomide analogs: Design, synthesis and biological evaluation.

9. AM Alaa, AS El-Azab, AM Alanazi, YA Asiri, IA Al-Suwaidan, et al. (2016) Synthesis and potential antitumor activity of 7-(4-substituted piperazin-1-yl)-4-oxoquinolines based on ciprofloxacin and norfloxacin scaffolds: in silico studies 31(5):796-809.
10. MK Ibrahim, AEA El-Helby, AH Ghiaty, AH Biomy, AA Abd-El Rahman Modeling, Synthesis And Antihyperglycemic Activity Of Novel Quinazolinones Containing Sulfonylurea.
11. IA Al-Suwaidan, AAM Abdel-Aziz, TZ Shower, RR Ayyad, AM Alanazi, et al. (2016) Synthesis, antitumor activity and molecular docking study of some novel 3-benzyl-4 (3H) quinazolinone analogues Journal of enzyme inhibition and medicinal chemistry 31(1): 78-89.
12. K El-Adl, AGA El-Helby, RR Ayyad, HA Mahdy, MM Khalifa, et al. Design, synthesis, and anti-proliferative evaluation of new quinazolin-4 (3H)-ones as potential VEGFR-2 inhibitors Bioorganic & Medicinal Chemistry 29: 115872.
13. AAM Abdel-Aziz, AS El-Azab, AM Alanazi, YA Asiri, IA Al-Suwaidan, et al. (2016) Synthesis and potential antitumor activity of 7-(4-substituted piperazin-1-yl)-4-oxoquinolines based on ciprofloxacin and norfloxacin scaffolds: in silico studies Journal of Enzyme Inhibition and Medicinal Chemistry 31(5): 796-809.
14. AGA El-Helby, RR Ayyad, HM Sakr, AS Abdelrahim, K El-Adl, et al. (2017) Design, synthesis, molecular modeling and biological evaluation of novel 2, 3-dihydrophthalazine-1, 4-dione derivatives as potential anticonvulsant agents Journal of Molecular Structure 1130: 333-351.
15. AM Alanazi, AAM Abdel-Aziz, TZ Shower, RR Ayyad, AM Al-Obaid, et al. (2016) Synthesis, antitumor and antimicrobial activity of some new 6-methyl-3-phenyl-4(3H)-quinazolinone analogues: in silico studies Journal of Enzyme Inhibition and Medicinal Chemistry 31(5): 721-735.
16. IH Eissa, AM Metwaly, A Belal, ABM Mehany, RR Ayyad, et al. (2019) Discovery and antiproliferative evaluation of new quinoxalines as potential DNA intercalators and topoisomerase II inhibitors Archiv der Pharmazie 352(11): 1900123.
17. AGA El-Helby, RRA Ayyad, H Sakr, K El-Adl, MM Ali, et al. (2017) design, synthesis, molecular docking, and anticancer activity of phthalazine derivatives as VEGFR-2 inhibitors Archiv der Pharmazie 350(12): 1700240.
18. AGA El-Helby, H Sakr, RR Ayyad, HA Mahdy, MM Khalifa, et al. (2020) Design, synthesis, molecular modeling, in vivo studies and anticancer activity evaluation of new phthalazine derivatives as potential DNA intercalators and topoisomerase II ... Bioorganic chemistry 103: 104233.
19. AM Alaa, AS El-Azab, LA Abou-Zeid, KEH ElTahir, NI Abdel-Aziz, et al. (2020) Synthesis, anti-inflammatory, analgesic and COX-1/2 inhibition activities of anilides based on 5, 5-diphenylimidazolidine-2, 4-dione scaffold: molecular docking studies European journal of medicinal chemistry 115: 121-131.
20. AGA El-Helby, RRA Ayyad, MF Zayed, HS Abulkhair, H Elkady, et al. (2019) Design, synthesis, in silico ADMET profile and GABA-A docking of novel phthalazines as potent anticonvulsants Archiv Der Pharmazie 352(5): 1800387.
21. AGA El-Helby, RRA Ayyad, K El-Adl, H Elkady (2019) Phthalazine-1, 4-dione derivatives as non-competitive AMPA receptor antagonists: design, synthesis, anticonvulsant evaluation, ADMET profile and molecular docking Molecular diversity 23: 283-298.
22. MK Ibrahim, AA Abd-Elrahman, RRA Ayyad, K El-Adl, AM Mansour, et al. (2013) (Design and synthesis of some novel 2-(3-methyl-2-oxoquinoxalin-1 (2H)-yl)-N-(4-(substituted) phenyl) acetamide derivatives for biological evaluation as anticonvulsant agents Bulletin of Faculty of Pharmacy, Cairo University 51(1): 101-111.
23. AS El-Azab, AM Alaa, RR Ayyad, M Ceruso, CT Supuran (2016) Inhibition of carbonic anhydrase isoforms I, II, IV, VII and XII with carboxylates and sulfonamides incorporating phthalimide/phthalic anhydride scaffolds Bioorganic & medicinal chemistry 24 (1), 20-25.
24. K El-Adl, AGA El-Helby, H Sakr, RR Ayyad, HA Mahdy, et al. (2021) Design, synthesis, molecular docking, anticancer evaluations, and in silico pharmacokinetic studies of novel 5- [(4-chloro/2, 4-dichloro) benzylidene] thiazolidine-2, 4-dione ... Archiv der Pharmazie 354(2): 2000279.
25. AGA El-Helby, H Sakr, RRA Ayyad, K El-Adl, MM Ali, et al. (2018) Design, synthesis, in vitro anti-cancer activity, ADMET profile and molecular docking of novel triazolo [3, 4-a] phthalazine derivatives targeting VEGFR-2 enzyme Anti-Cancer Agents in Medicinal Chemistry 18(8): 1184-1196.
26. AA Elhelby, RR Ayyad, MF Zayed (2011) Synthesis and biological evaluation of some novel quinoxaline derivatives as anticonvulsant agents Arzneimittelforschung 61(07): 379-381.
27. T Al-Warhi, AM El Kerdawy, N Aljaeed, OE Ismael, RR Ayyad, et al. (2020) Synthesis, biological evaluation and in silico studies of certain oxindole-indole conjugates as anticancer CDK inhibitors Molecules 25(9): 2031.
28. AGA El-Helby, RRA Ayyad, K El-Adl, H Sakr, AA Abd-Elrahman, IH Eissa, et al. Design, molecular docking and synthesis of some novel 4-acetyl-1-substituted-3,4-dihydroquinoxalin-2(1H)-one derivatives for anticonvulsant evaluation as AMPA ... Medicinal Chemistry Research 25: 3030-3046.
29. AGA El-Helby, RRA Ayyad, K El-Adl, A Elwan (2017) Quinoxalin-2(1H)-one derived AMPA-receptor antagonists: Design, synthesis, molecular docking and anticonvulsant activity Medicinal Chemistry Research 26: 2967-2984.
30. WM Eldehna, R Salem, ZM Elsayed, T Al-Warhi, HR Knany, et al. Development of novel benzofuran-isatin conjugates as potential antiproliferative agents with apoptosis inducing mechanism in Colon cancer Journal of Enzyme Inhibition and Medicinal Chemistry 36(1): 1423-1434.
31. MM Khalifa, HM Sakr, A Ibrahim, AM Mansour, RR Ayyad (2022) Design and synthesis of new benzylidene-quinazolinone hybrids as potential anti-diabetic agents: In vitro  $\alpha$ -glucosidase inhibition, and docking studies Journal of Molecular Structure 1250: 131768.
32. WM Eldehna, MF Abo-Ashour, T Al-Warhi, ST Al-Rashood, A Alharbi, et al. Development of 2-oxindolin-3-ylidene-indole-3-carbohydrazide derivatives as novel apoptotic and anti-proliferative agents towards colorectal cancer cells Journal of Enzyme Inhibition and Medicinal Chemistry 36(1): 320-329.
33. MF Zayed, RR Ayyad Some novel anticonvulsant agents derived from phthalazinedione Arzneimittelforschung 62(11): 532-536.
34. AA El-Helby, MK Ibrahim, AA Abdel-Rahman, RRA Ayyad, MA Menshawy, et al. (2022) Synthesis, molecular modeling and anticonvulsant activity of benzoxazole derivatives Al-Azhar J Pharm Sci 40: 252-70.
35. H Sakr, RR Ayyad, AA El-Helby, MM Khalifa, HA Mahdy (2021) Discovery of novel triazolophthalazine derivatives as DNA intercalators and topoisomerase II inhibitors Archiv der Pharmazie 354(6): 2000456.
36. AGA El-Helby, H Sakr, RRA Ayyad, K El-Adl, MM Ali, et al. Anti-Cancer Agents Med Chem 18(8): 1184.
37. RRA Ayyad, H Sakr, K El-Gamal (2016) Synthesis, modeling, and anticonvulsant activity of some phthalazinone derivatives American Journal of Organic Chemistry 6(1): 29-38.

38. RR Ayyad, HM Sakr, KM El-Gamal, IH Eissa, A HA, et al. Anti-Inflammatory, Proton Pump Inhibitor and Synthesis of Some New Benzimidazole Derivatives *Der Chemica Sinica* 8(1): 184-197.
39. E Nassar, YA El-Badry, AMM Eltoukhy, RR Ayyad. Synthesis and Antiproliferative Activity of 1-(4-(1H-Indol-3-Yl)-6-(4-Methoxyphenyl) Pyrimidin-2-yl) Hydrazine and Its Pyrazolo Pyrimidine Derivatives *Med chem (Los Angeles)* 6: 224-233.
40. R Ayyad (2012) Synthesis and Biological Evaluation of Novel Iodophthalazinedione Derivatives as Anticonvulsant Agents *Al-Azhar Journal of Pharmaceutical Sciences* 45(1): 1-13.
41. T Al-Warhi, H Almahli, RM Maklad, ZM Elsayed, MA El Hassab, et al. (2023) 1-Benzyl-5-bromo-3-hydranoindolin-2-ones as Novel Anticancer Agents: Synthesis, Biological Evaluation and Molecular Modeling *Insights Molecules* 28 (7), 3203.
42. M Salem, R Ayyad, H Sakr (2022) Design and Synthesis of Some New Oxadiazole Derivatives as Anticancer Agents *International Journal of Organic Chemistry* 12(02): 64-74.
43. H M Sakr, RR Ayyad, K Mahmoud, A M Mansour, G Ahmed (2021) Design, Synthesis of Analgesics and Anticancer of Some New Derivatives of Benzimidazole *International Journal of Organic Chemistry* 11(03): 144-169.
44. RA Ayyad, HM Sakr, KM El-Gamal (2016) Design, Synthesis, Computer Modeling and Analgesic Activity of Some New Disubstituted Quinazolin-4 (3H)-ones *Med. Chem* 6(5): 299-305.
45. R Ayyad (2014) Synthesis and Anticonvulsant Activity of 6-Iodo Phthalazinedione Derivatives *Al-Azhar Journal of Pharmaceutical Sciences* 50(2): 43-54.



This work is licensed under Creative Commons Attribution 4.0 License  
DOI: [10.19080/OMCIJ.2023.13.555861](https://doi.org/10.19080/OMCIJ.2023.13.555861)

### Your next submission with Juniper Publishers will reach you the below assets

- Quality Editorial service
- Swift Peer Review
- Reprints availability
- E-prints Service
- Manuscript Podcast for convenient understanding
- Global attainment for your research
- Manuscript accessibility in different formats  
( Pdf, E-pub, Full Text, Audio)
- Unceasing customer service

Track the below URL for one-step submission

<https://juniperpublishers.com/online-submission.php>