Preparation, Characterization and Study of Biological Activities of New Organozinc Compounds Drived from Cytosine

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Abstract

The novel heterocyclic organozinc compounds were prepared from the reaction of diazonum salt cytosine zinc chloride with thymol and vanilin as coupler components. The prepared compounds were characterized by elemental analysis and UV-Vis, FTIR and ^{1}HMNR spectroscopic techniques. The biological activity was also studied for all prepared compounds.

Keyword: Organzic, Azo cytosine, Perparation, Identification ,Biological activity.

Introduction

Now day, organozinc compound represents the largest and is an indispensable part of synthetic chemist's knowledge [1]. It has received much attention due to the fact that almost every synthesis of natural product has at least one step which contains the use of this type of compounds. So, there is constant need for the development of new method for a simple and effective synthesis organozinc compound [2]. For organozinc bivalent two basic types (R_2Zn and R Zn X) where R being hydrocarbon groups or more generally groups attached to zinc via a zinc-carbon bond and X being a halogen or groups being attached to zinc(oxygen, nitrogen, sulphar, phosphorus and the like). Furthermore organozinc compounds are strongly electron-deficient since four low-lying orbitals are available for bonding and only two valance electrons are supplied by zinc [3]. Zinc (II) compounds have been adopted several coordination geometries commonly octahedral, tetrahedral and various penta coordinate geometries, so these structural flexibility can be attributed to zinc's electronic configuration [Ar] $3d^{10}4s^2$. The 3d subshell is filled and therefore, ligand field effects, it does not exist [4]. Thus the coordination geometry is determined largely by electrostatic and steric interactions [5]. This type of compounds have been widely employed in many applications such as in clinical, biological and industrial [6,7]. In addition the rich chemistry of the azo compounds are associated with several applications, e.g. industrial, dyeing and biological reactions [8,10] with histochemical detection of compounds containing cytosine moiety. This paper describes the synthesis organozinc compounds include azo moiety. Identification and biological activity were studied for prepared compounds.

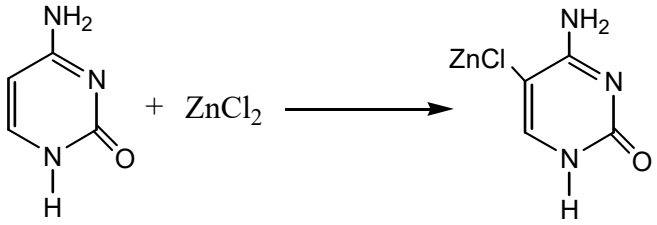
Experimental

Materials and Instrument

All solvent and chemicals were used directly as purchased. UV-Vis spectra were recorded on a (shimadzn uv-160 A) Ultra Videt-Visible spectrophotometer. FTIR-Spectra were taken on a (shimadzn, FTIR-8400s Fourier Transfor, Infrared) Spectrophotometer (200-4000) cm^{-1} with samples prepared as CsI discs. The ^{1}HNMR spectra were recorded on (Brucker-300 MHz Ultra shield) using DMSO as a solvent and TMS as a reference. Melting points were obtained by using (Stuart Melting Point Apparatus). Microelemental analysis (C, H ,N) were performed by using (Euro vector EA 3000A Elemental Analyser). The percentage of (Zn) was determined by A.A using a (GBC 933) Flame Atomic Absorption Spectrophotometer.The Cl% was determined by Mohr method.

Preparation Method

Cytosine zinc chloride was prepared from the reaction of cytosine with zinc chloride according to literature [11] as was shown below:



Preparation of (C_1 & C_2)

(0.01 mole) of cytosine zinc chloride was dissolved in a mixture of 2 ml H_2SO_4 (conc.), 10ml ethanol and 10ml distilled water. After that this solution diazotized at (0-5)°C with 2.5% sodium nitrite solution. The diazo solution was added dropwise with stirring to a cooled alkaline ethanolic solution of (0.01 mole) of vanilin and thymol . Color precipitate was

filtered and washed several times with (1:1) EtOH:H_2O, mixture then left to dry. The reaction is shown below

Result and Discussion

The two color compounds ($C_1$and C_2) were prepared by coupling thymol and vanillin respectively with diazonium solution of cytosinezinc(II) chloride. They are not soluble in water but soluble in most organic solvent (ethanol , chloroform, carbontetrachloride ,DMF, … etc) and are stable in air, moisture and light. The elemental analysis data and physical properties are included in Table (1).

The synthesized compounds (C_1 and C_2) were characterized by UV-Vis, FTIR and ^{1}HNMR spectroscopy.

UV-Vis Spectra

The prepared compounds (C_1 and C_2) were characterized by UV-Vis spectroscopic technique in ethanol (10^{-3} M) as shown in Figure (1 and 2) which were mainly showed two peaks, the first peak at (365,420nm) for (C_1 and C_2) respectively were assigned to a ($\pi\rightarrow\pi^*$) transition of benzene ring and substituted functional group, so they cause a very pronounced shift and a greatly intensified absorption [12]. The second band which was observed in the region (612nm and517nm) (Table1) for (C_1 and C_2) respectively, due to ($\pi\rightarrow\pi^*$) transition of intermolecular charge transfer involving the whole electronic system through azo moiety [13].

FTIR Spectra

The important vibrational bands have been determined on the basis of t he reported assignments of IR spectral bonds in the literature [14-16].The FTIR spectrum for (C_1) (Figure 3) exhibited a strong and sharp band at (3498 cm $^{-1}$) with shoulder at (3479 cm $^{-1}$), which is assignable to ν(OH) on the thymol ring while in the spectrum of (C_2) (Figure 4) was observed a broad medium intensity band in the region (3581-3400 cm^{-1}) and centered at (3490 cm $^{-1}$)that attributed to the (O-H) stretching vibration of internally hydrogen bonded enolic group[17]. Thus, the FTIR spectrum strongly supports the existence of an intra molecular hydrogen bond azo-enol form. Theν(N-H) in the pyrimidyl moiety was observed at (3402 and 3303 cm^{-1}) in the spectra for ($C_1$and C_2) respectively, the changes in shape and position of this band were presumably due to formation of new azo compound boarding of the band in (C_2). The (C_1 and C_2) were exhibited a medium duplet band at (1604, 1585cm^{-1}) and (1676, 1649) cm^{-1}respectively which were assignable to $\nu(C{=}O)_{ald.+pym.}$ and $\nu(C{=}N)_{pym.}$. The band for the

ν(N=N) appeared with broading and shifted to low wave number in the spectrum of (C_1 and C_2) at (1483, 1450 cm^{-1}) and (1455, 1404 cm^{-1}) respectively may be due to the intramolecular interaction between nitrogen atom for azo moiety and zinc atom (N–Zn) in the solid state [18]. At (1311 cm^{-1}) in the spectrum for (C_2) referred to the ν(C–O) for the aldehyde group the vanillin moiety. Intermolecular interaction for ν(N–Zn) at (459 and 452 cm^{-1}) and ν(Zn–Cl) at (229 and 230 cm^{-1}) for (C_1 and C_2) respectively [14, 18]. The characteristic bands for (C_1 and C_2) are given in Table (2). These data are in agreement with these earlier reported.

^{1}HNMR Spectra

Figure (5) showed the ^{1}HNMR spectrum for the compound (C_1), it was observed different peaks. A singlet signal at δ(9.18, 1H)ppm referred to the (–NH) for the proton of pyrimidine moiety and multiplet signal at δ(7.9- 7.1, 3H)ppm. The singlet signal also appeared at δ(4-6, 1H)ppm and (3.13, 9H)ppm which corresponded to the phenolic proton (OH) and methyl protons respectively. However the ^{1}HNMR spectrum for compound (C_2) (Figure 6) showed a singlet signal at δ(9.93, 1H)ppm, (9.11, 1H)ppm, (6.7, 1H)ppm and (4.78, 3H)ppm for (CHO), $(N–H)_{pyr.}$, $(O–H)_{ph.}$ and $(O–CH_3)$ respectively. The benzene ring was observed multiplet signal at δ(7.9-7.2) ppm [15,19].

Antibacterial Activity

Due to well known antibiotic properties for these kinds of compounds [20,21], they exhibit a variety biological activities. The antibacterial activities of the prepared compounds (C_1 and C_2) have been studied against three selected types of bacteria *Escherichia Coli, Staphylococcus Aursea* and *Bacillus*. The paper disc diffusion method has been used and the activity was determined by measuring the diameter of the zone of inhibition in mm. Tetracycline was used as standard material in order to make a comparison of it's effectiveness with that at the prepared compounds (C_1 and C_2) and ethanol was used as a solvent, while the concentration of solution was (10^{-4}M). Table(3) shows that the (C_1) has high activity against selected bacteria while (C_2) appeared different activity which was recorded.

Conclusion

The obtained from elemental analysis, UV-Vis, FTIR and ^{1}HNMR spectroscopy indicated and characterized two new hetrocyclicorgan zinc compounds that prepared by coupling reaction of vaniline and thymol with diazonium salt of cytosine zinc chloride.

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Table (1): Physical properties and elemental analysis for $C_1$and C_2

Compound	Color (λ_{max})nm	MWt.	Yield%	M.P.	Eemental analysis (Cal.)				
					C%	H%	N%	M%	Cl%
C_1	Blue(612)	374.12	86	295	44.66 (44.67)	3.701 (3.72)	14.87 (14.89)	17.32 (17.38)	9.34 (9.44)
C_2	Red(517)	376.03	83	310	40.88 (40.95)	2.36 (2.39)	14.87 (14.89)	17.36 (17.38)	9.43 (9.44)

Table (2): The main FTIR bands (200-4000) cm^{-1} for (C_1 and C_2) Compounds

compounds	ν(OH)	ν(N–H)	ν(C–H)$_{arm.+alk.}$	ν(C=O)$_{ald.=im}$ ν(C=N)$_{im}$	ν(N=N)	ν(C–O)	ν(N–Zn)	ν(Zn–Cl)
C_1	3498st, sh 3479vw,shl	3402 vw	3099 w 2954 w	1604m 1585m	1483 sh,st 1450 sh,m	–	459 w	229 m
C_2	3581 3400	3303 w,br	3064 vw 2883 vw	1676m 1649m	1455m 1404m	1311 w	452 w	230 m

vw=very weak, w=weak; m=medium, st=strong; sh=sharp, br=broad, shl=shoulder, d=dublet

Table (3): Antibacterial activity for (C_1 and C_2)

compounds	*E.Coli*	*S.auerus*	*Bacillus*
C_1	+++	+++	+++
C_2	++	+++	++
Tetracycline	+++	+++	+++

++ (7-9)mm, +++ (10-12)mm

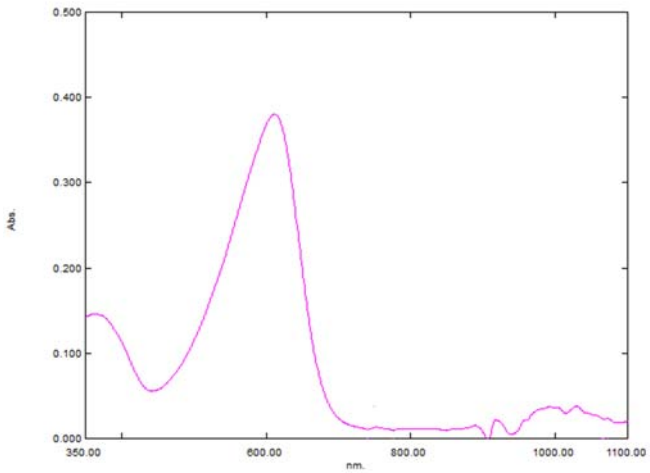

Figure (1): The electronic spectrum of C_1 compound

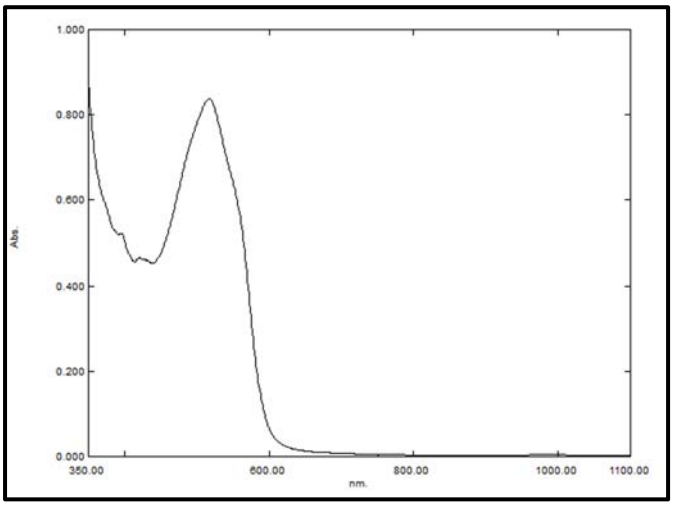

Figure (2): The electronic spectrum of C_2 compound

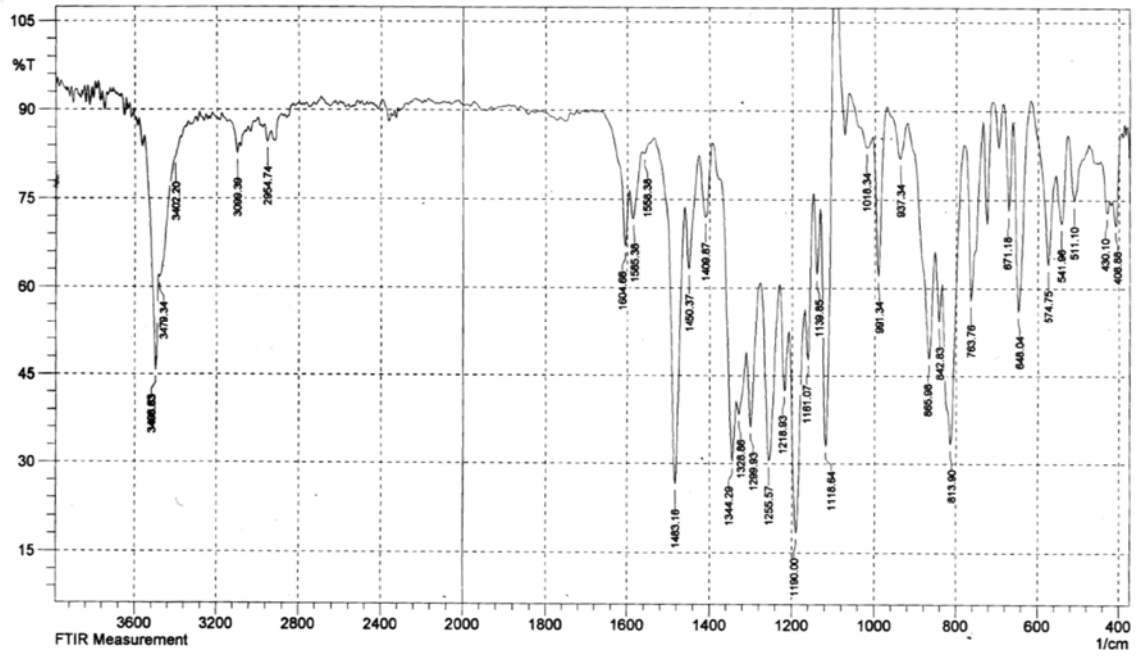

Figure (3): FTIR spectrum for (C_1) compound

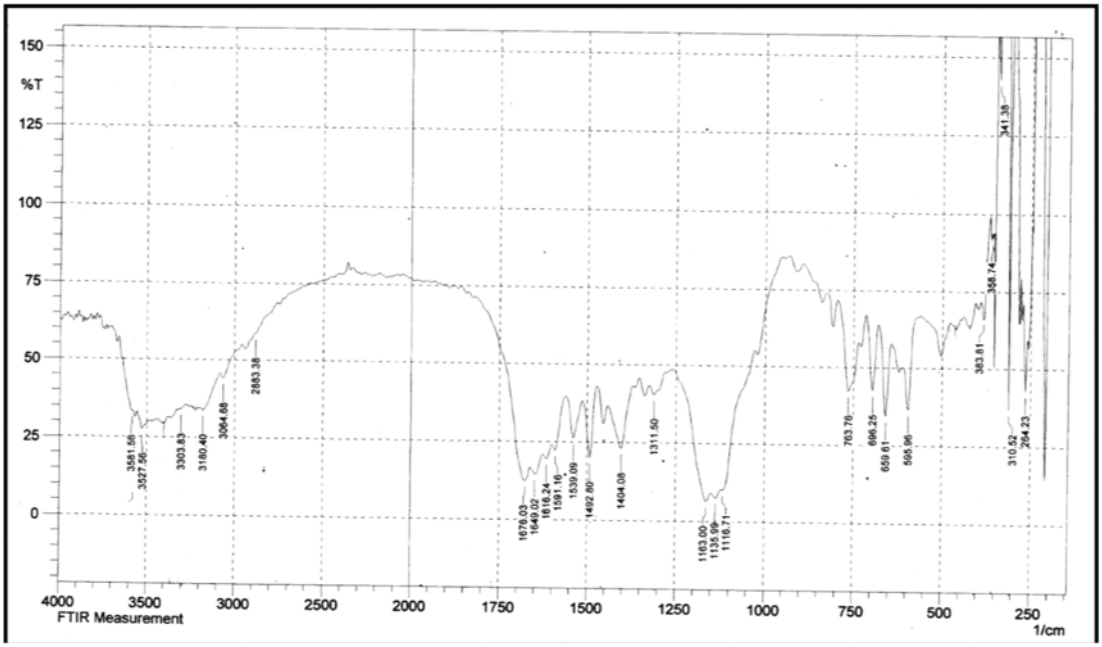

Figure (4): FTIR spectrum for (C_2) compound

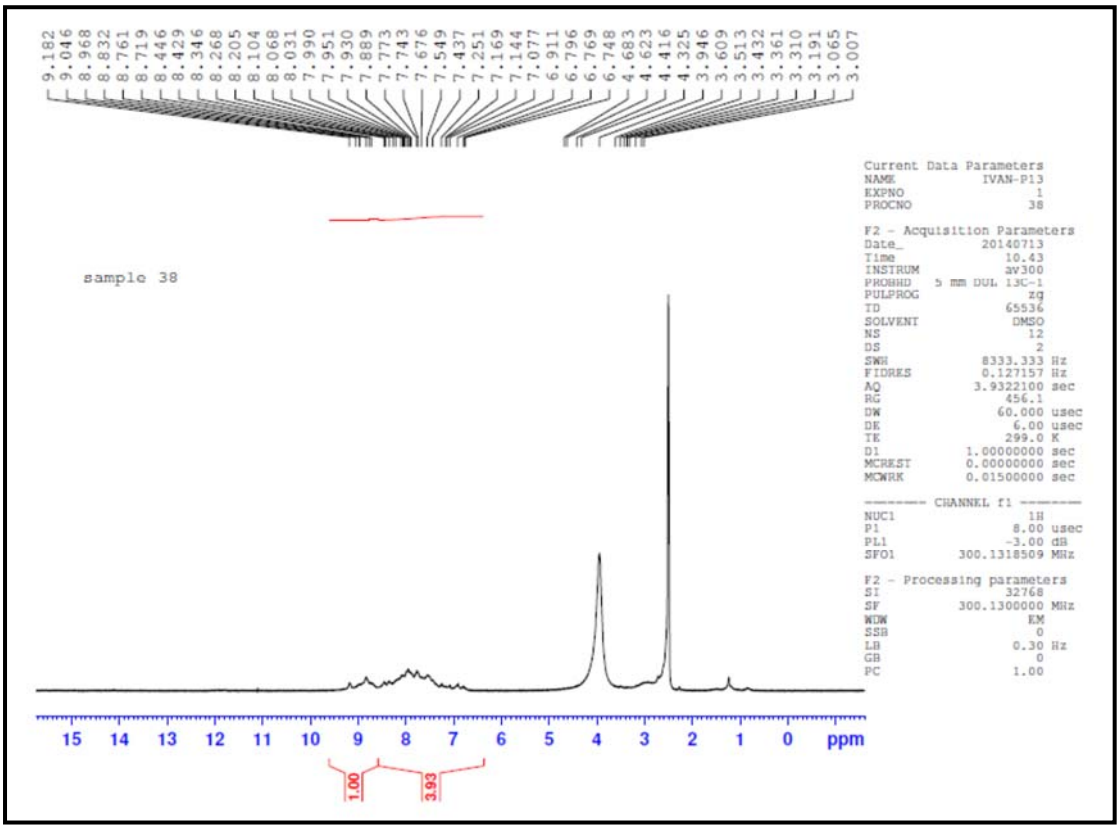

Figure (5): The HNMR spectrum for C_1 compound

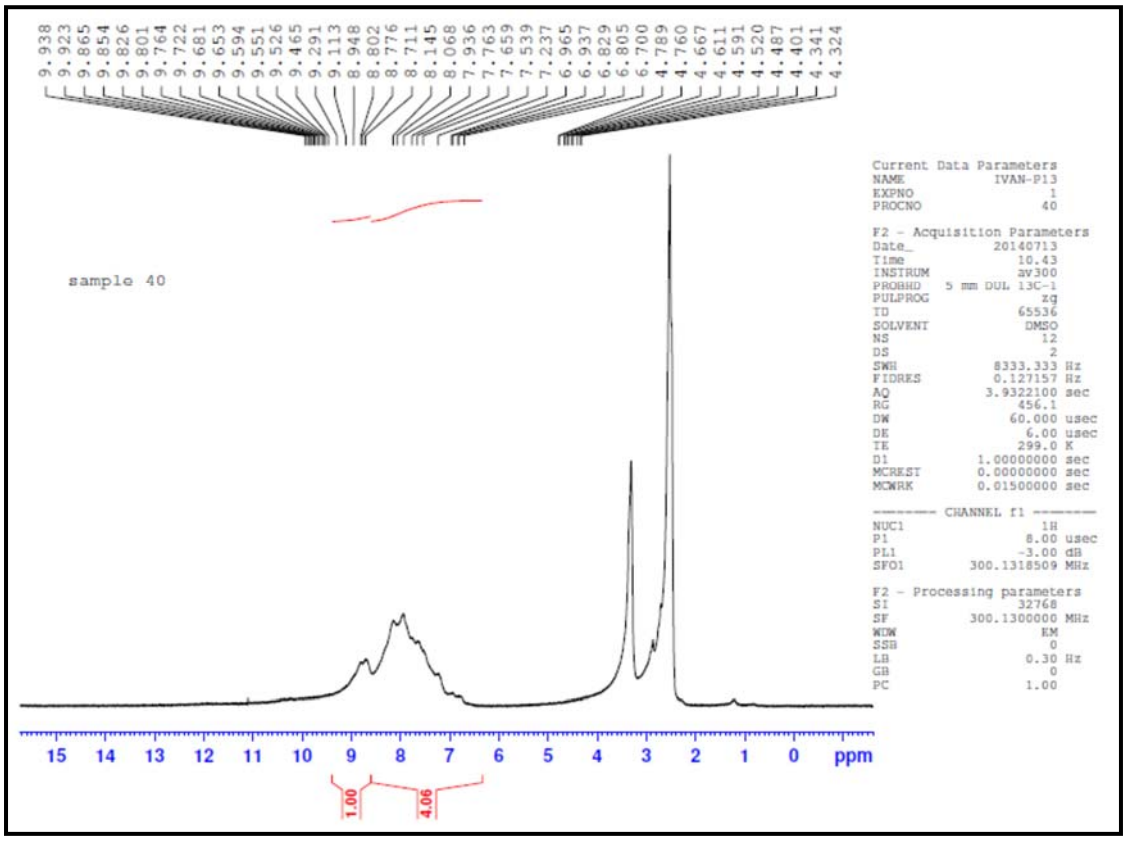

Figure (6): The ^{1}HNMR spectrum for C_2 compound

تحضير وتشخيص ودراسة الفعالية البايولوجية لمركبات زنك – عضوية جديدة مشتقة من السايتوسين

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استلم في:17/تشرين الثاني/ 2015 ،قبل في:31/كانون الثاني/2016

الخلاصة

حضرت مركبات عضوية فلزية للزنك جديدة و ذلك من تفاعل ملح الدايزونيوم لكلوريد الزنك سيتوسين مع الثايمول و الفانيلين مكونة ازدواج المركبات المحضرة شخصت بوساطة دراسة اطياف الاشعة فوق البنفسجية-المرئية والاشعة التحت الحمراء و الرنين النووي المغناطيسي. اظهرت هذه المركبات فعالية بايولوجية ضد انواع منتخبة من البكتريا.

الكلمات المفتاحية : زنك عضوية, آزو سايتوسين , تحضير , تشخيص , فعالية بايولوجية