

Synthesis and Characterization of a Novel Biological Mixed Organometallic Chromium (III) Complex of Potential Allyl -Sulfur Compounds of Garlic, Allicin.



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Abstract

From the readily acid and base hydrolysis (pH – dependence) of loosely Cr – S bond of bis (L- cysteinato)chromium (III) complexes, a biological mixed organometallic – Werner chromium complex, of trans - bis $[(\eta^3) S - \text{allyl mercapto cysteinato}]$ chromium (III) hydroxide, has been synthesized via intermolecular insertion reaction of allyl sulfenic acid, which was extracted and isolated from natural garlic. This complex was characterized using IR, NMR, UV -Visible spectroscopic techniques and elemental analysis. Also biological activity of the prepared complex was tested in vitro.

Keyword:- Chromium (III), Organometallic, Garlic. Allicin.

Introduction

Garlic (*Allium sativum*) has been used all over the world for more than thousand years both for cooking and medical purpose. Medical studies (1-16) have showed that garlic can lower high blood pressure, prevent dangerous blood clots, lower cholesterol, prevent cancer, protect against bacterial and fungal infections, kill parasitic worms. Scientists concluded that the health related properties of garlic are attributed to organosulfur compounds, particularly to allicin, the pungent odor compound that is not originally present in raw – garlic bulb. Allicin is formed directly after crushing, slicing and chopping of garlic by enzymatic reaction of alliin by alliinase. However, allicin was thought to be the garlic principal potential ingredient, but now researches proved that allicin is highly unstable reactive/oxidative compound, which decomposes and reacts yield other sulfur containing biological compounds (11-13). Therefore, after the extraction processing the extra ordering benefits of garlic components were established and registered by researchers (3-6). These sulfur-containing compounds were classified based on their volatility and solubility as oil (odorous) and water (odorless) soluble compound (14). Now it has been well known that

raw garlic contains unstable substances. Common food processing creates compounds that are not essentially present in raw garlic amongst allicin.

Allicin (s-diallyl thio sulfenate) the main chemical sulfurs constituent of garlic, when it is released possess a strong odor and it has powerful pharmacological properties. Experimental evidence proved this in vitro testing since 1940. Allicin has been extracted from crushed cloves of wet and aging garlic. The GC and HPLC with mass spectrometer techniques have been employed for its separation and identification (17). Also its isolation from alliin and alliinase was performed by enzymatic reaction. The TLC and HPLC have been used for both analysis and quantitative determination of allicin (17). In laboratory, allicin was synthesized from diallyldisulfide oxidation by H_2O_2 in acid medium (18). This healthy giving component of garlic, allicin, has been synthesized newly and mixed with reusable substances that stabilize the garlic enzyme alliinase in order to restore without losing its effectiveness (19). Exclusive processes have been used to retain nearly all garlic constituents in their natural conditions and stabilize them until their consumption (19). Now, the allicine unsuitability became a fact, and changes into other compounds in few days. It is crucial that allicin and alliin with alliinase could be stabilized to the place where in the body can effectively be used.

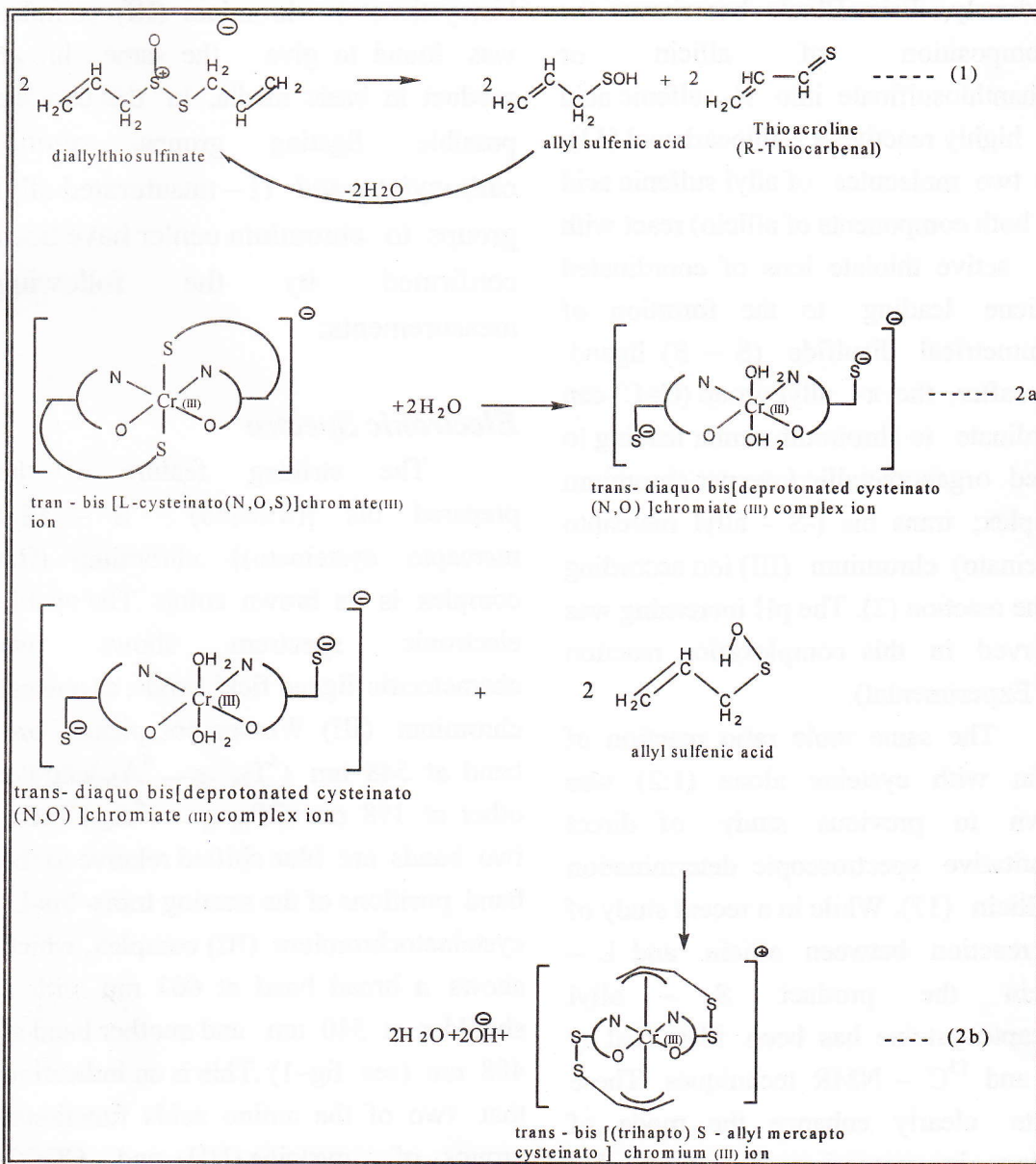
However, the mechanism of biological and biochemical of allicin action is not known in detail. Two possible mechanisms of its action were suggested; the antioxidant of allicin and interaction reaction with other compounds containing thiolate group to form S – S compounds. The interaction reaction of allicin and cysteine or other organosulfur containing compounds have been studied (20). Researchers suggested that the anti – oxidant properties of allicin alone can not show its biological and biochemical activities but S – H modifying of allicin was found to be more significant for its activity. In the aim of the elucidating the interaction reaction mechanism of the allicin and its precursor alliin, some chromium (III) complexes of potential allyl – sulfur-containing compounds of natural garlic have been synthesized and their invitro biological activities have been studied.

Results and Discussion

The prominent color change of bis- cysteinato chromium (III) complex, which include loosely poor bonded Cr – S, was observed in acid and base hydrolysis. This change is due to cleavage of both Cr – S bonds leading to free thiolato ions (RS^-) in near physiological media ($RS - H$ group in acidic media) (21). These free thiolato ions prompted us to undertake the current study of the intermolecular insertion reaction of some sulfur containing compounds of allicin

into this active thiolate group of bis-cysteinato chromium (III) complex, in order to prepare some mixed organo metallic / Werner chromium (III) complexes. Up to date no one attached any significant to such type of chromium (III) complexes. This complex is

produced from the direct reaction of the decomposed allacin (diallyl thio sulfinate, $C_3H_5S(O)SC_3H_5$), with trans- diaquo bis [deprotonated cystenao (N,O)] chromium (III) complex from hydrolysis trans – bis(cystienato) chromate (III) ion, according to the following scheme.



In the reaction (1), two molecules of alliin decompose to two molecules of allyl sulfenic acid (which combine in a reversible condensation reaction to alliin) and two molecules unsaturated thio carbenals ($\text{RC}=\text{S}$) (11,20). Previously, Eric Block has shown the decomposition of alliin or methanthiosulfinate into R- sulfenic acid and highly reactive R - thiocarbenal (11). The two molecules of allyl sulfenic acid (or both components of alliin) react with two active thiolate ions of coordinated cysteine leading to the formation of asymmetrical disulfide (S - S) ligand. Thereafter, the π - allyl group ($\text{C}=\text{C}$) can coordinate to chromium center leading to mixed organometallic / werner chromium complex; trans bis (-S - allyl mercapto cysteinato) chromium (III) ion according to the reaction (2). The pH increasing was observed in this complexation reaction (see Experimental).

The same mole ratio reaction of alliin with cysteine alone (1:2) was shown in previous study of direct quantitative spectroscopic determination of alliin (17). While in a recent study of the reaction between alliin and L - cysteine the product S - allyl mercaptocysteine has been identified by ^1H and ^{13}C - NMR techniques. These results clearly enhance the mode of binding in preparing the trans bis

[(trinepto)- S - allylmercaptocysteinato] chromium (III) complex. The reaction of sulfur containing compounds of natural garlic (both water and alcohol extracts) and also prepared alliin according to published procedure (18) with trans-bis(cystienato) chromium (III) complex was found to give the same brown product in basic media. In this case the possible ligating groups, amino, carboxylato and Π - unsaturated allyl groups to chromium center have been confirmed by the following measurements:

Electronic Spectra

The striking feature of the prepared bis [(trihapto) S - allyl mercapto cysteinato]- chromium (III) complex is its brown color. The visible electronic spectrum shows two characteristic ligand field bands, as a usual chromium (III) Werner complexes, one band at 548 nm ($^4\text{T}_{2g} \leftarrow ^4\text{A}_{2g}$) and the other at 398 nm ($^4\text{T}_{1g} \leftarrow ^4\text{A}_{2g}$). These two bands are blue shifted relative to the band positions of the starting trans- bis-L- cysteinatochromium (III) complex, which shows a broad band at 603 nm with a shoulder at 540 nm and another band at 408 nm (see fig-1). This is an indication that two of the amino acids functional groups of cysteine, (NH_2 and COO^-)

remain in the coordinated sphere. The loosely Cr – S bond cleavage occurs upon hydrolysis which gives a sulfenato ion. Scavenging the charge transfer band in ultraviolet at 258 nm (C T) for Cr-S also assists this result and in stead of this, a band at 242 nm is appeared. This band has been assigned to either the coordinated allyl (unsaturated groups (C=C) charge transfer band (22) or to the selective absorption of disulfide (S-S) in vicinity of chromium center.

Infrared Spectra

IR – spectra of the starting reacted compounds and that of products have been measured in the range 400 – 4400 cm^{-1} and their characteristic bands are tabulated in table (1). A band $\nu_{690} \text{cm}^{-1}$ is assigned to Cr-S bond in bis-cysteinatoChromium (III) complex was disappeared upon hydrolysis, because it is replaced by allyl (C=C) group. The IR-spectra of the synthesized, bis (S- allyl mercaptocysteinato) chromium (III) hydroxide and the starting complex, bis (cysteinato) chromium (III) exhibit characteristic bands at 1407cm^{-1} , 1660cm^{-1} and 1420cm^{-1} , 1650cm^{-1} , which are assigned to sym, and asym $\nu_{\text{C=O}}$ stretching frequencies respectively. While the free carboxyl group of the free cysteine or glycine was found at 1430cm^{-1} and 1670cm^{-1} . This shows that these bands in both IR spectra of the complexes were red shifted according to the explanation shown by Nakamoto (32). Also a band corresponding to $\nu_{\text{Cr-O}}$ was found in both complex spectra at $540\text{-}550 \text{cm}^{-1}$. These results confirm that carboxyl group of the cysteinato remains coordinated through oxygen to the chromium center (32). Also IR- spectra of the above two complexes have a broad band corresponding to $\nu_{\text{N-H}}$ at 3230cm^{-1} and 3225cm^{-1} respectively. While the amino group frequency in glycine and

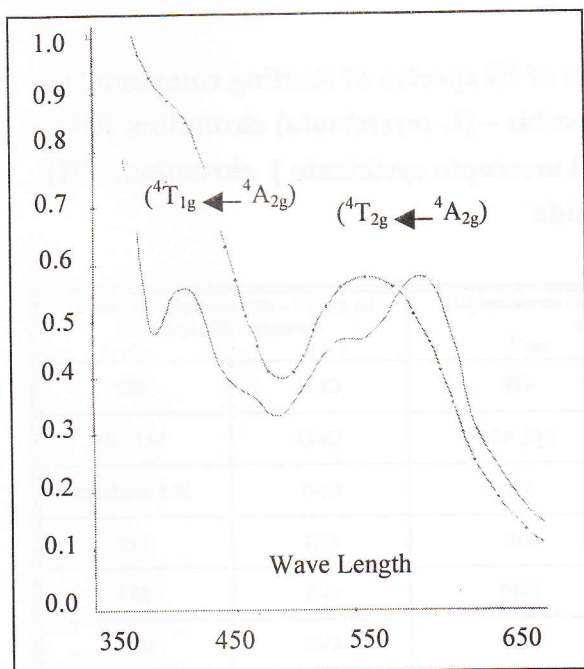


Fig (1) The Viible electronic spectra of (- . -) bis – [(trihapto)- s- allyl marcapto L-cysteinato]chromium (III) complex and (—) trans bis (cysteinato) chromium (III).

cysteine appeared in the range 2600- 3100 cm^{-1} . This also indicates that amino group remains coordinated in both complexes. This result was supported by the presence of $\nu\text{Cr-N}$ at 478 cm^{-1} in the spectra of both complexes. Scavenging the band assigned to $\nu\text{Cr-S}$ at 690 cm^{-1} supports the suggested hydrolysis of Cr-bond as mentioned above. While a band at 610 cm^{-1} assigned to $\nu\text{C-S}$ band in non-coordinated sulfur of the cysteinato chromium (III) complex was found in product spectra. This bond frequency is resulted from the blue shifting of the

coordinated sulfur ($\nu\text{C-S}$ at 670 cm^{-1}), which may be explained on the basis that the sulfur atom forms a disulfide with the decomposed allicin compound. Also the $\nu\text{C-S}$ band of disulfide was observed at 611 cm^{-1} (see table -1). An attracting point was the similarity of the spectra of both extracted (water and alcohol) and synthesized allicin having a characteristic broad band (νOH) at 3140 cm^{-1} , which assigns to SOH group of the decomposed product of allicin (or its precursor) under our experimental condition (see table -1).

Table (1) Some characteristic bands of IR spectra of starting compounds, water and alcohol extracts of garlic, sodium bis - [L-(cysteinato) chromium (III) dihydrate complex (I) and bis $[(\eta^3)\text{S} - \text{allyl mercapto cysteinato}]$ chromium (III) hydroxide

Garlic; (Alcohol extract) (Water extract)		sodium bis - (L-cysteinato) chromium(III) dihydrate (I)		bis $[(\eta^3)\text{S} - \text{allyl mercapto cysteinato}]$ chromium (III) hydroxide (II)	
cm^{-1}	cm^{-1}		cm^{-1}		cm^{-1}
S-S	554 550	Cr-N	478	Cr-N	480
C-S	611 610	Cr-O	542, 408	Cr-O	547,410
O.O.P bend C-H	939 930	Cr-S	690	Cr-S	Not available
C=S	1030 1026	C-S	670	C-S	610
S=O	1060 1050	C-N	1040	S-S	550
C-O	1144 1140	C=O sy	1420	C-N	1030
C=C	1660 1660	C=O asy	1660	C-O	1137
C-H str	2940 2940	C-O	1137	C=Osy	1407
O-H	3366 3366	C-H str	2956	C=Oasy	1650
		N-Hstr	3225	N-Hstr	3230
				O-H	3410

NMR – Spectra

The allyl group of coordinated disulfide ligand (S-allylmercapto cysteinato) can linked to chromium center either through unsaturated (C=C) or delocalized electrons of all three MOs of carbon atoms of the group, in the inner sphere of the prepared complex. The NMR spectra of an intermediate (violet color) of dihydroxy di-S allylmercapto cysteinato chromium (III) complex (see later), in which C=C group is not coordinated and that of the complex bis(-S allyl mercapto cysteinato) chromium(III) complex (brown color), in which C=C group is linked to Cr center, were shown in Fig (2) and Fig (3) respectively. Consider the spectrum in Fig (2), the resonance signals are very similar to that of free the vinyl signals and appeared typically at 2.25, 2.6, 3.8, 6.2, 9.18 δ (21). But all the signals are shifted to a relatively strong shielded side after coordination of the allyl group and appeared as coalesced band at (2.7, δ) and a doublet at (5.58 δ) by the affect of chromium atom. This result is quiet well agree with that found for expected shift of organo aren chromium compounds (22,23) and on other side allows to suggest that the allyl groups are all involved in binding to chromium center as (trihepto). Recently evidence has also been obtained in our laboratory that diallyl disulfide substituted via allyl group interaction, while saturated

dialkyldisulfide does not adherent to the chromium atom (24).

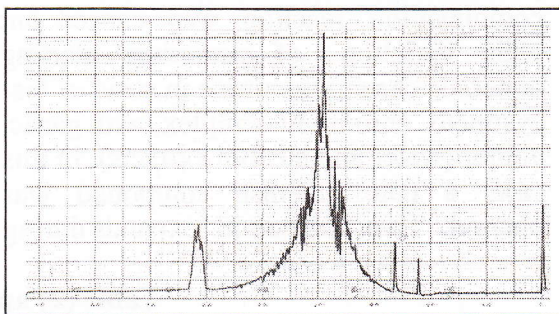


Fig – 2 – NMR Spectrum of intermediate (violet color) diaquo bis-S-allyl mercapto L- cysteinato chromium (III) complex in DMSO

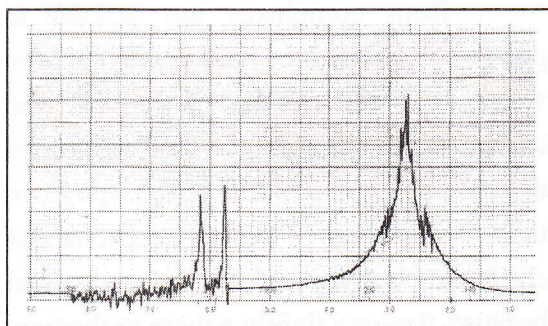


Fig -3- NMR Spectrum of trans - bis [(η^3) S – allyl mercapto L cysteinato] chromium (III) hydroxide complex in DMSO

Elemental Analysis

The prepared complexes, were analyzed for C,H,N and S with Cr. The results were tabulated in table (2). These results and some other physical properties afford the general formula, $[\text{Cr}(\text{C}_6\text{H}_{10}\text{N}_2\text{O}_2\text{S}_2)_2]\text{OH}$, bis [(η^3) - S-allyl mercapto L - cysteinato] chromium (III) hydroxide, for the prepared complex from the reaction of bis-cystineto chromium

complex and garlic, allicin (water and alcohol extracts) in near physiological pHs. While in acid media the complexation reaction was carried out with variation of chromium starting material; chromium nitrate in stead of bis-cystineto chromium complex, with garlic, allicin (water and alcohol extracts). In this case a pale greenish compound was obtained. This compound expands during

its formation as sphagnum. Elemental analysis (see table -2) and some other tests for sulfur show that sulfur was not detectable. Upon this results the general formula $[\text{Cr}(\text{C}_3\text{H}_4\text{O})_3(\text{H}_2\text{O})_3](\text{NO}_3)_3$, tri aquo tri propenal chromium (III) nitrate was suggested. However the color was observed to change to yellow brown upon standing for a long period of time or by increasing the pH to basic media.

Table (2) analytical results

Compounds	color	% C		% H		% N		% Cr
		Found	Calculate	Found	Calculate	Found	Calculate	Found
$\text{Na}[\text{Cr}(\text{C}_3\text{H}_5\text{O}_2\text{NS})_2] \cdot 2\text{H}_2\text{O}$ (I)	blue	20.75	20.6	4.5	4.0	8.01	8.02	15.1
$\text{Cr}[(\text{C}_6\text{H}_{10}\text{NOS}_2)_2]\text{OH}$, (II)	brown	33.5	31.78	5.6	4.63	6.36	6.18	12.1
$[\text{Cr}(\text{C}_3\text{H}_4\text{O})_3(\text{H}_2\text{O})_3](\text{NO}_3)_3$ (III)	pale green	22.7	23.48	3.43	3.91	10.08	9.13	11.6

Both complexes are soluble in polar solvent and they are very soluble in water, which shows that they are charged compounds. Attempts were made to determine the magnitude of the charge on these complexes by using ion exchanger chromatography, were unsuccessful because they are tightly adhere to the tope of ion exchange resin.

But the prepared complexes were tested for biological activity, the data were recorded in table- 3, which shows that only bis $[(\eta^3)\text{-S-allyl mercapto L-cysteinato}]$ chromium (III) hydroxide complex has (+ve) response in vitro biological test against microorganisims, E. coli and staphylococcus at room temperature, atypical result against a challenge was showed in fig(4).

Upon previous discussion in the current study two conclusions could be drown;

1. The loosely Cr -S bond is kinetically liable, contrary to the behavior inert chromium (III) (d^3), and readily hydrolysis to give a very active deprotonated thiolate (RS⁻) ion, near physiological pHs. If the chromium - sulfur amino acid cysteine complex, contains cysteinato ligand, which coordinates through amine and carboxylate groups (glycine like mode), there will be a free deprotonated thiolate available for insertion reaction with other sulfur containing compounds leading to disulfide (S-S) product near physiological pH. As mentioned before the garlic allicin(or its precursor alliin), which possesses a power of biological and clinical therapeutic characters due to sulfur-containing compounds in its chemical structure, can form such disulfide. On the other hand the properties

of the thiol – chromium bonding interests chemists mainly from the point of view that facilitating this thiol-thiol formation interaction reaction (25). So, the results of the current study allow to suggest the mechanism for this thiol-thiol formation reaction, of the sulfur containing

compound of garlic allicin (or its constituents) and the active site of deprotonated thiolate (RS⁻) of coordinated L-cysteine in aqueous media (near physiological pHs), may result according to the following scheme:

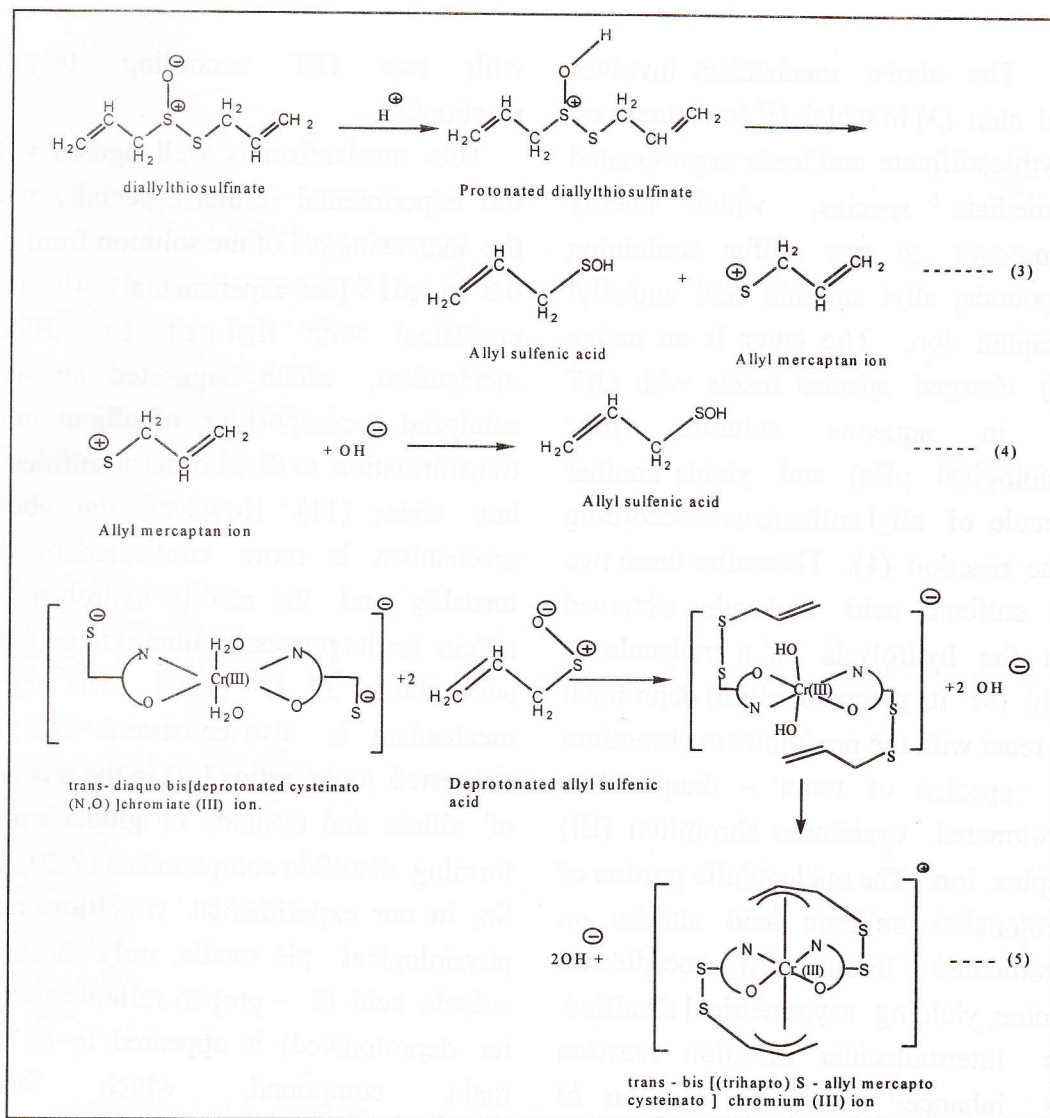


Table (3) Anti microbial activity of prepared complexes

complexes	Staphylococcus	E.coli
bis [(η ³) S – allyl mercapto cysteinato] chromium (III) hydroxide	(+)ve	(+)ve
Tri aqua tri propenal chromium(III)	(-)ve	(-)ve
Control	(-)ve	(-)ve

(+)Ve: Inhibit the growth of anti microbial, (-) Ve : No inhibition, Control : Disk of (KBr)

The above mechanism involves initial step (3) in which H⁺ ion attacks on diallythiosulfinate and leads to protonated intermediate species, which readily decomposes to two sulfur containing compounds; allyl sulfenic acid and allyl mercaptan ion. The latter is an active (+ve) charged species reacts with OH⁻ ion, in aqueous solution (near physiological pHs) and yields another molecule of allyl sulfenic acid according to the reaction (4). Thereafter these two allyl sulfenic acid molecules obtained from the hydrolysis of a molecule of allicin (or its precursor alliin) deprotonat and react with the predominant chromium (III) species of trans – diaquo bis-deprotonated cysteinato chromium (III) complex ion. The nucleophilic portion of deprotonated sulfenic acid attacks on deprotonated thiolat of coordinated cysteine yielding asymmetrical disulfied. This intermolecular insertion reaction may inhance substitution reaction of activated allyl moiety to bind to chromium center and gives eventually trans- bis (trihapto)S-allylmercaptocyeinato chromium (III) ion

with two OH⁻ according to the reaction(5).

This mechanism is well agreed with the experimental results especially with the increasing pH of the solution from pH 6.5 to pH 9 (see experimental). Also it is consistent with that of Eric Block mechanism, which suggested an acid catalyzed decomposition of allicin in its transformation to di, tri or tetra sulfides in hot water (11). However, the above mechanism is more confirmed by the unstably and the readily hydrolysis of allicin (or its processor allicin) to sulfenic acid above 37 C⁰ (11C). The above mechanism is also consistent with the suggested mole ratio (1:2) in the reaction of allicin and cysteine or glutathion in forming disulfide compounds. (17,20,27). So, in our experimental conditions near physiological pH media, only the allyl sulfenic acid (2 – propen sulfenic acid or its deprotonated) is appeared to be the main compound, which forms asymmetrical disulfied with deprotonated thiolate of cysteine. The biological and biochemical activities of allicin (or its constituents) also may be result from this

SOH modification in forming disulfide compounds.

2. Both water and alcohol (in temperate temperature) extracts of natural garlic and the synthesized allicin react with bis-cysteinato chromium (III) complex. The both yield the same brown colored complex, of trans - bis [(trihepto) S - allyl mercapto cysteinato chromium (III) ion, with the total charge one (+ve) ion, in near physiological pH. This also provides support to the above mechanism and assist previous suggestion that sulfenic acid is the main reacting species. However both allicin and it precursor alliin contain allyl sulfenic acid in their structures, when they decompose in aqueous media give deprotonated allyl sulfenic near physiological PH. While these deprotonated thiolate species does not exist in acidic media ($pH < 5$). The protonated thiolate (RSH) species of both the complex and the allyl sulfenic acid are prevailing in acidic media, they can not react according to the above mechanism to yield brown product complex. However, the reaction mixture of garlic extracts (water and alcohol) with chromium (III) nitrate reacts in acidic media ($pH=2$) yielding different color and charged complex, in which sulfur atom has not been detected. The biological response has been observed only for synthesized sulfur contain complex, this may result from presence the S - allyl mercapto cysteine, which arises from the hydrolysis of complex in the incubated system. This sulfur amino acid compound

contains both (S-S) linkage and allyl moiety, which has been shown to have biological and chemoprotective activity against some carcinogenic chemicals and also to have competitive inhibitor character invitro tests (14,27,28). Now our aim is to further characterize the synthesized complexes and to conduct kinetic studies and thermodynamic stability of these complex formation in order to give better understanding of allicin and other allyl sulfur containing compounds in garlic extracts, in addition to the chromium role in biological system.

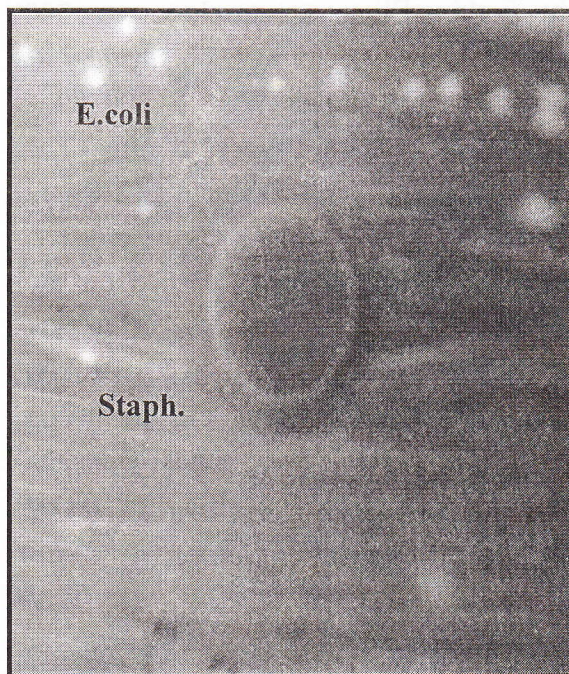


Fig. - 4- A typical challenge against growth of the two anti microbial; staphylococcus and E.coli

Experimental

Chemical reagents; Chromium (III) nitrate, Potassium hydrogen carbonate, silver nitrate and organic solvents were obtained from Riedel De Hanaen Seelze –Hannover, L-cysteine, ninhydrine were obtained from Fluke-Garanite, and diallyl disulfide was obtained from KOCH – light laboratories LTD., England. All are analytical grades used without purification. Garlic was purchased from local market.

Electronic spectra were measured by Perkin Elmer spectrophotometer 200 Hetachi. IR – spectra were obtained by IR – spectrophotometer WQF – 300 FT – optical instrument factory, Beijing. The NMR spectra were obtained by Hetachi Perkin Elmer R – 24B 60MHz. Chromium analysis was carried out by Atomic absorption method, using AA spectrophotometer WFX – 120. BRAIC and also by following the published procedure (31). The other elements analysis C,H,N and S were carried out by an Iraqi oil Exploration Company.

Synthesis of Trans Biscysteinato Chromium (III) Complex

This complex was prepared by following the procedure, with slight modification of De Messeter et al.(30). A solution of chromium nitrate (2.5×10^{-3} mol.) in 15 ml H_2O was mixed with the

solution of cystein (7.5×10^{-3} mol.) in 10 ml water. The resulting mixture was boiled for a few minutes and then $NaCO_3$ was added to adjust the pH of solution of pH 8, at which mixture turn blue color. After cooling in ice a blue crystal precipitate was filtered off. The precipitate was washed with ethanol and acetone, then dried by diethyl ether.

Synthesis of Allicin

The allicin was synthesized by H_2O_2 oxidation of diallyl disulfide according to published procedure by Mayenx et.al. (18) and purified on silica gel column (230–400 mesh) using 15% ethyl acetate and hexane as elution solvent. The solvent was evaporated by rotator evaporation under vacuum.

Extraction and Isolation of Alliin and Allicin

The extraction and isolation allicin and its precursor alliin from garlic were carried out by two different procedures as following:

(i) Extraction and isolation at temperate temperature (alcoholic extract). The sliced and crushed garlic cloves of frizzed garlic (25 gm) was soaked in 100 ml methanol (80%) for 48 hrs. The methanol was replaced twice each time by (100 ml). Then the mixture was filtrated and concentrated by rotary vacuum evaporator. The concentrated

was mixed drop by drop with 150 ml 40% ethanol and water. The mixture was left for 24hrs and filtered. The filtrate was concentrated in vacuum again. The residue was mixed with 15 ml of ice cold methanol and left at (0 C°) for 2 hrs. The white crystal was obtained and filtered off. This was washed with small volume of diethyl ether and ice cold methanol. This white precipitate changes to pale yellow crystals (~ 1 gm), which is soluble in 40% ethanol and its melting point is 164 C°. This pale yellow crystal was more purified by column chromatography on silica gel (250 mesh) using 40% ethanol as elution solvent. The eluting portions were collected and evaporated by vacuum rotator evaporator, eventually yield white color needle crystals with m.p.164 C°. Thin layer, chromatography (TLC) identification with mixture (n – butanol, n – propanol , glacial acetic acid and water mixture) (3:1:1:1 v/v) was carried out on the precouted silica gel plates, then the dried plates were sprayed with ninhydrine, three spots were obtained however two spots were found with chromium trioxide – glacial, acetic acid (Rf 0.19 and 0.125), corresponding to the two stereoscopic products of alliin (18).

(ii) Extraction and isolation of alliin and allicin constituents (water extract):

In room temperature (300 gm) of garlic was sliced and crushed by coffee machine and put on soxhelt then extracted

with distilled water for 3 hrs. The water extract was filtered and the yellow oily filtrate was transferred to a large evaporating dish and left for 24hrs in a dry dark hood. The yellow needle crystals (m.p.95 –100 C°) were obtained, and washed with ether. TLC test as mentioned before gives three constituents when the dried plates were developed with ninhydrin and gives two spots with chromium trioxide – glacial, acetic acid (Rf 0.19 and 0.43), that are corresponding to alliin and allicin constituents, allyl sulfuenic acid.

Synthesis of Trans-bis (s – allyl mercaptocysienato) Chromium (III) Hydroxide Complex

A calculated amount of sodium salt trans – bis (cysteinato chromium (III) hydrate, Na [(Cr (cyst)₂ 2H₂O)], (0.77 x 10⁻³ mol) was dissolved in 10 ml H₂O. This solution (pH~ 7.5) was mixed with (0.25 gm) of either water or alcohol extracts (allicin from garlic) or synthesized allicin in 15 ml H₂O (pH~ 6.5). The mixture was refluxed for 3hrs until the color of the solution converted from blue to red violet color. The pH of mixture was observed to increase to ~ pH 9, with continuing reflux for another 3 hrs, brown crystal was obtained. This crystal was filtered off and washed with ice water and ethanol and dried with ether, it has m.p 114- 115 C°.

References

- [1] E.Dorant, Van den, P.A. Brandtt., R.A .Goldbohm, R.J. Hermns and F. Sturman "Garlic and its significance for the prevention of cancer in humans", *acritical view, Br.J.cancer* ,1993,67(3),424-9.
- [2] D.B. Foushee, J. Ruffin, U. Banerjee "Garlic potential role in reducing heart disease", *Br. J. Clin .Pract* . 1993,47(2),64-5.
- [3] C. Legnani, M. Frascaro, G. Guazzaloca, S. Ludovici , G.Cesarano and S. Cocche "Thioally compound potent inhibitors of cell proliferation" ,*Biochim Biophys Acta*, 1994 ,1221(1), 73-7.
- [4] (a) S. Sutabhaha, M.Suttajitm, "Antitumor effects of organosulfur compounds present in garlic against canine mammary tumor cell", *FASEBJ*, 1992, 6(4), 1391.
(b) S.G. Sundaram, J.A. Milner "Impact of organosulfur compounds in garlic on canine mammary tumor cells in culture", *cancer lett.*1993 ,74(1-2) , 85-90.
- [5] Great Bear Communications, Inc. at Intoegreat bear, (net Copy right), 1996, 1997 sect 1, Volum 2. "Garlic Allium Sativuum family": *Liliaceae*.
- [6] Herbal information center, "Gralic" *Herbs Seite* 1998 1.Von 3, Seit 3, Von 3.
- [7] "A clove of Garlic or Health and Cookery, Recipes and Traditions, Garlic Natures" Super Healer by Joan wilen and Lydia Wilen ; 1996.
- [8] R.Gebhardt "Inhibition of Cholesterol Biosynthesis by Water – Soluble Garlic extracts", *Drug Res.*1992,41,800-804
- [9] The Nutrition Reporter "The Wander of Garlic" 1996, Seite 2, von.4.
- [10] F.Freeman, Y.Kodera "Garlic Chemistry; Stability of allicin in blood, solvents and simulated physiological fluids", *J. Agri and Food Chemistry*; 1995, 43,2332-2338.
- [11] (a) E. Block "The Organo Sulfur Chemistry of the Genus Allium –Implications for organic chemistry of sulfur", *Angew chem. Int.Ed.Engl*, 1992, 31,1135-1178.
(b) E.Block "The chemistry of garlic and onion", *Scientific American*, 1985, 252, 114-119.
(c) E.Block, S.Ahmad, J.L.Catatfamo, M.Kjain and R.A.Castro. "Anti thrombotic Orgaosulfur compounds from garlis", *J.Am. Chem. Sco.* 1986, 108, 7045.
- [12] T.H Yu and C.M Wu "Stability of allicin in garlic Juice" , *J.Food Sci* ,1989 54,977-981
- [13] Kyollic information.Volum (1)and Volum (2) of Kyolic Scientific Information, *seite 3 Von3 and seite 4_Von 5* 1997.
- [14] S.Nakagawa, Masamoto, K.Sumiyson "Effect of Raw garlic extract on growth of young rats and their oranges after petraral administration", *J.Toxical Sc.*1980, 5,91-112
- [15] J.A. Lyborser, J.S Gallagher, D.W Pulver "Occupational Asthma Induced by Inhalation and Ingestion of garlic", *J.Allergy Clin. Immunol*, 1982 69,448.
- [16] L. Lawson, D.K Ransom and Hughes "Inhibition of Whole Blood platelet Aggregation by compound in garlic" ,*Thrombosis research*,1992, 65 , 141-156.
- [17] (a) H.Joam, L.Lawson, Grace Han "A spectrophotometric Method for Quantitative Determination of Allicin and Total Garlic Thiosulfinates" ,*Analytical Biochemistry Chem J*;Super criteal ,1995.
(b) "Fluid Chromatography of garlic extracts with mass spectrometric identification of allicin", *J Chromatogr.Sci.*1994, 23(3) , 248-400.

- [18] (a) A. Stoll, E. Seebeck "Chemical investigation of allicin, the specific principle of garlic", *Ad. Enzymol*, 1951, **11**, 377-400.
(b) P.R. Mayeux, K.C. Agrawal, J.S.H. Tou, B.T. King, G.L. Lipton, A.L. Hyman, D.B. M. Namara "The pharmacological effects of allicin, a constituent of garlic", *Agents and Actions*, 1988, **25**, 182-190
- [19] APIC USA, Inc. Amino Acids, Herbs, A primer on the chemistry of Garlic (1998) and Herb Glossaries, 1997, *Action*, 1988, **25**, 201-209.
- [20] R. Aharon M. Talia, K. Leonid, W. Meir, M. David and Levweiner "The mode of Action of Allicin Trapping of radicals and interaction with thiol containing proteins", *J. Biochemica Biophysica Acta*, 1998, **1379**, 233-244.
- [21] (a) P. O'Brien, J.P. Jesus and T.M. Santo "A kinetic and equilibrium study of the reaction of potassium and sodium bis L-cysteinate (N,O,S) – chromium (III) in moderately acidic solution", *Inorg. Chem. Acta* 1987, **131**; 5 – 7.
(b) M.A. Abdullah and B.H. Abdullah "Kinetic studies of the ring closure reaction of sodium bis (L-cysteinate chromate (III) in neutral aqueous solution", *Iraqi J. of chem*, 1998, **24**, (2), 233.
- [22] E.O. Fisher and H. Branner, *Chem. Ber* 1956, **98**, 175.
- [23] R.P.A. Sneed, "Organochromium compounds" academics press a subsidiary of Harcourt Brace, Jovanovich, publisher 1975, ch.2, 97.
- [24] P. Powell. "Principle of organometallic chemistry" Ch. 8. 253, 1988.
- [25] M.A. Abdullah, manuscript submitted for publication "Synthesis and characterization of new class of mixed polysulfide ligand with chromium (III) complexes" 2000.
- [26] (a) M.E. Dion, M. Ager, J.A. Milner, "S-allyl Cysteine inhibits nitrosomorpholin formation and bioactivation", *Nutr. Cancer*, 1997, **28(1)**, 1-6.
(b) J.T. Pinto, C. Qiao, J. Xing, R.S. Rivlin, M.L. Protomastro., M.L. Weissler, X. Tao, H. Thaler and W.D. Heston "Effect of garlic thioallyl derivatives on growth, glutathione concentration and polyamine formation of human prostate carcinoma cells in culture", *HmJ.clin.Nutr.* 1997, **66(2)**, 398-405.
- [27] J. Barrett and P. O'Brien and J.D. Pedrosa. "Chromium (III) and Glucose Tolerance Factor", *polyhedron*, 1985, **4(1)**, 1-14.
- [28] (a) David Hoffman, M.N.I.M.H "garlic" (1995),
(b) M.T. Tradfer, M.A. Ali, N. Saravanan, W.Y. Weng, S. Kumar, "Coordination Chemistry and biological activity of two tridentate ONS and NNS Schiff bases", *Transition Metal Chemistry*, 2000, **25** (3), 295.
- [29] F.G.R. Gimbiatt "Inorganic polymer chemistry" P. 219 – 230 and 399 – 411 1963.
- [30] P. de Meester, D.J. Hodgson, F.C. Freeman and C.J. Moore, "Tridentate Coordination by the L-Cysteine Dianion, Crystal and Molecular structure of sodium Bis (L-Cysteinate) chromate (III) dihydrate", *Inorg. Chem.* 1977, **16**, 1494.
- [31] T.L. Allen, "Spectrophotometer Chromium Determination, *Analytical Chemistry*", 1958, **30(3)**, 447-449.
- [32] K. Nakamoto, *Infrared and Raman spectra of Inorganic Compounds*; John Wiley and Sons; New York 3rd ed 1977, 305.

ئامادەکردنی و ناسینەوهی ئاویتەیی ئالۆزیکى نۆی بایۆلۆجى كرۆم (III) تیکەلاوی ئۆرگانۆمیتەلی بەئەلایەلی سیر - ئەلیسین

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پوختە

لەم لیکۆلینەوهیەدا ئالۆزیکى بایۆلۆجى كرۆم (III) تیکەلاوی ئۆرگانۆمیتەلی / ویرنەری
trans - bis [(trihapto) - s - allyl mercaptocysteinato (N,O)] chromium (III) hydroxide
ئامادەکرا بە کارلیکی هەلۆهشانەوهی ئاوی بەندیکی لاوی (Cr - S) لە ئاویتەیی ئالۆزی - L
bis (L - cyctenato O,N,S) chromate (III) وه ئاویتەیی allylsulfenic ی لە سیری سروشتی دەرھینراو)
ئەلیسین و پیکھاتەکانی (بە پیکە چۆنەناو و بەندبوونی کیمیا. بەرپیکە شیکردنەوهی شەبەنگی
تیشگی بینراو و سەر و وەنەوشەیی و ژێر سوور و لەرینەوهی موگناتیسی ناوکی وه بەرپیکە شیتەلی
کردنەوهی ووردی توخمەکان ناسراو تەوه و دیاری کراوه.

تخزیر و تشخیز معقد عضوی الكروم كرۆم (III) الجید و النشط بايولوجيا من خلیط عضوی ثلاثي هايپوكبريداليل الثوم - الالیسین

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الخلاصة

في هذه الدراسة تم تخزیر مركب جدید لمعقد كروم (III) النشطة بايولوجيا وهي مركب عضوی
فلزي ویرنر trans - bis [(trihapto) - s - allyl mercapto cycteinato (N,O)] chromium (III) hydroxide
من تفاعل مباشر بين الناتج من التحلل المائي لأصرة (Cr - S) في المعقد كروم - L
bis (L - cyctenato O,N,S) chromate (III) والمركب allylsulfenic المستخلصة من الثوم الطبيعي (التي
تتضمن الیسین ومكوناته) بطريقة التدخل والربط الكيمياء، وتم تشخیز الناتج بواسطة التحلل الدقیق
للعناصر وطرق الاطياف لأشعة فوق البنفسجية والمرئية وتحت الحمراء والرنين النووي المغناطيسي.

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