Available online www.jocpr.com

Journal of Chemical and Pharmaceutical Research, 2012, 4(1):209-215



Research Article

ISSN: 0975-7384 CODEN(USA): JCPRC5

Review on Biochemical Importance of Vitamin-U

Asha D. Patel and N. K. Prajapati

Department of Chemistry, M. N. College, Visnagar, Mehsana (Gujarat), India

ABSTRACT

In this article, a comparatively less known molecule vitamin-U has been described. The chemical characteristics of this rare vitamin has been described. Clinical studies carried out using this molecule, biological significance including metabolic characteristics; cholesterol lowering properties, biosynthesis etc. have been described. General characteristics and complexing behaviour of this molecule is discussed in the article.

Key words: vitamin-U, Methyl methionine sulfonium chloride, biochemical significance.

, ,

INTRODUCTION

'Vitamin U' is one of the most rare vitamins. Brassico therapy or therapy using cabbage sources of vitamin U has been applied since ancient times. Hyppocrates, the father of medicine, applied it to his patients. In 1998, a new preparation was developed from a special red-cabbage. (coalis lombarda) was processed bio-organically, guaranteeing a high quality vitamin. Vitamin U was originally used for the substance, later found to be vitamin Bc and not be a bacterial growth factor that could be a derivatives of folacin. The prime food source appears to be raw cabbage 'vitamin U' is the anti-ulcer vitamin reported in cabbage leaves and other green vegetables.[1-3]. It has been used for its reputed protective effect on the liver and gastro-intestinal mucosa and thus used in the treatment of gastric disorders. 'Vitamin U' has a beneficial power action on gastric and intestinal functions in general. It has a cytoprotective mechanism which may possibly be related to surface mucosal mucin. It stimulates the formation of various categories of RNA and causes a quantitative increase in the RNA temperature function. Vitamin U, also known as S-methyl methionine was found to increase activity of S-adenosyl-L-homocysteine. This decrease the inhibition of S-adenosyl-L-homocystein and stimulates methylation process. 'vitamin U' is recommended for treating oesophagogastric lesions, chronic gastric ulceration, chronic gastritis, ulcerative colitis, diaphragmatic hernias and peptic ulcers.' Vitamin U'is also recommended as a preventive vitamin for the digestive and intestinal systems. The vitamin U concentrations in fruits of citrus hybrids were measured, and found to increase during ripening of the fruit. Crossbreeding is useful in producing new citrus fruits that have juices with the desirable characteristics of their parents without formation of dimethylsulfide which is an off- flavor [4].

Chemical Characteristics

The gas-chromatographic method of analysis of vitamin U is based on the disintegration of vitamin U in the alkaline medium to form equimolecular quantities of dimethylsulphide and homoserine [5]. A method, based on electrophoretic measurement has been developed by Khuchua. This method includes extraction, purification and treating with cation exchanger and is followed by eluation with 2N NaOH. This is measured spectrophotometrically at 506 nm [6]. Leung developed a high-performance liquid chromatographic method for the determination of vitamin U in tablets and capsules. Threonine was employed as the internal standard through the assay. The ophthalaldehyde derivatives were prepared and then chromatographed isocratically on a reversed-phase C18 column. The optimum reaction time for both, vitamin U and threonine at pH 10.5 is 5 min. Vitamin U and its major degradation product in the dosage forms , viz., methioninesulphoxide , were separated and quantified with a relative

standard deviation of about 1%, using a fluorescence detector with excitation and emission wavelengths at 340 and 450 nm respectively [7]. A pre-column derivatization method for the high-performance liquid chromatographic determination of taurine (1), L-glutamine (2), vitamin U (3) and L-aspartic acid (4) in pharmaceuticals has been developed by Uehara et. al. The optimum requirements for the derivatization conditions and the stability of resulting derivatives were discussed [8]. Seri et. al. studied the hypolipidemic effects of vitamin U which were compared with clofibrate in three experimental procedures. In results, the characteristic effect of vitamin U is discussed through therapeutic viewpoint [9].

(Vitamin U) (Methyl methionine sulfonium chloride) (MMSC)

M.W = 199.70 gms M.F = $C_6H_{14}CINO_2S$ White needles, m.p. 134

Clinical Studies

In France, clinical studies were carried out on patients suffering from gastro duodenal ulcers, peptic ulcers, gastritis and gastroduodenltis, diaphragmatic hernias, and peptic oesophagitis, patients were 80% relieved from their pain. The therapeutic effect of vitamin U has been clinically proven. Medical researchers have also conducted successful tests in Germany, Italy, Japan and United states. In one trial of 100 patients with peptic ulcer treated with vitamin U, 86 percent of the patients experienced relief of pain without the continued use of any from of drug therapy and without frequent feedings of food. These patients also showed an accelerated healing time for both gastric and duodenal ulcers [10]. An interesting note is that cabbage juice is very rich in L-glutamine, once again lending credence to this true traditional folk remedy. Two groups of patients, in each of which approximately 10 percent had failed to respond well to the usual regimen, were studied one by Cheney [11]. The other by Gianelli and Bellafiore [12]. Most of the patients became asymptomatic for the first time on a diet to which had been added eggs, butter, peanut butter, lettuce, watercress, parsley, broccoli, romaine and avocadoes - all foods said to be rich in antiulcer factor. This antiulcer factor was designated vitamin U. The idea of the therapeutic potential of vegetable juices, consider the work of Garnett Cheney. He had 100 peptic ulcer patients drink a quart of raw cabbage juice daily. The patients reported dramatically less pain and x-ray examination confirmed fasten healing time. There was no other change in their diet, and they did not have drug therapy [13]. Cheney used cabbage juice to also treat gastric ulcers and duodenal ulcers. He clearly was onto something which he called vitamin U (for ulcer) for lack of a better name [14]. Chency knew of people who have utilized cabbage juice along with vegetarian diet and fasting to heal all forms of gastrointestinal diseases without drugs and without surgery [15-16]. The vitamin U was found to produce a marked antidepressant effect in depressive states of various classifications of diseases irrespectively of the duration of the depression phase or preceding treatment [17]. Sulphide toxicity in colonocytes is reversible by methyl donors. The efficiency of sulphide detoxification may be an important factor in the pathogenesis and treatment of ulcerative colitis for which s-adenosylmethionine 1,4 butane disulphonate may be of therapeutic value [18]. Vitamin U was found to increase activity of s-adenosyl – L – homocysteine hydrolase, selectively methylating the released homocysteine [19]. Vitamin U is ubiquitous in the tissues of flowering plants, but its precise function remains unknown [20]. The committing step in methionine and s-adenosyl - L - methionine (SAM) synthesis is catalyzed by cystathionine gamma-synthase (CGS) [21]. The effects of vitamin U on aminonucleoside-induced nephrotic hyperlipidemia in rats were investigated. The results suggest that vitamin U may be useful as single or combined therapy for human nephrotic syndrome and its related hyperlipidemia as a safety drug [22]. The influence of vitamin U on metabolism of nucleic acids in E. coli MRE-600 has been studied by Lebenkaet al. The influence of vitamin U was compared with that of methionine. Addition of vitamin U to the medium at the concentration of 2.7-10(-5) M increased the incorporation of 5-methyl-3H-thymidine into DNA by about 20% and the incorporation of 2-14C-uridine into the total RNA of the cells by about 47%. The electrophoretic separation of RNA in polyacrylamide gels showed that vitamin U stimulated the incorporation of the label into 4s, 5s, 16s and 23s RNA with different intensity. The highest stimulation of the label incorporation has been observed in 16s RNA [23]. Metabolism of vitamin U has been studied in rats. Biotransformation of this compound activity proceeds in the liver, kidneys and digestive tract. Metabolism of vitamin U in the liver and kidneys was found to proceed with via methylation of homocysteine with the formation of methionine and via enzymatic hydrolysis to dimethylsulfide and homoserine. In

the digestive tract, only the activity of s-methylmethioninesulphonium hydrolase was found. The physiological role of the metabolic routes under study is discussed [24]. The role of butyrate has already been established. DGL-glycyrrizinised licorice extracts and the sulphur derived vitamin U can also be used, and there is now an additional factor that can work from with in. As a specific food for health enhancing intestinal bacteria, it encourages the proliferation of active endogenous bacteria and leads to the formation of butyrate on site [25]. Specific nutrients are known to exert a positive physiological effect upon the intestinal membarns. Nutrients such as those mentioned previously, like Fos, butyric acid (as serine butyrate). Vitamin U and DGL licorice extracts are helpful other factor such as N.A.G. (N-Acetyl Glycosamine); Zinc assorbate magnesium ascorbate and vitamin A have a direct role in helping to heal the intestinal membarns [25].

Biological Significance of Vitamin U

Cabbage extract factor, also known as vitamin U, has been extensively studied as a source of anti-peptic ulcer dietary factor. Results of a number of experiments carried out in the medical research laboratories at Standard University medical school indicate than an identified dietary factor plays some role on the etiology of peptic ulcer. [A] Bio Gastric: Watanabe et al developed the cytoprotective mechanism of vitamin U which may be mediated by sulfhydryl compounds, and the increase in surface mucosal mucin may possibly be related to cytoprotection [26]. Study of Watanabe et.al. showed that L-cysteine [Cys] and vitamin U inhibited ethanol- induced gastric mucosal damage and increased the amount of surface mucin in rates. This study examined whether Cys and vitamin U augmented mucin secretion and changed distribution of mucin vesicles ultrastructurally in mucous cells by using primary cultured mucous cells from rabbit glandular stomach. Change in intracellular cyclic adenosine 3', 5'-monophosphate (CAMP) and in levels of cytosolic free Ca⁺² were investigated by treatment with Cys and vitamin U. The present findings indicated that the increase in mucin secretion by Cys & vitamin U was not mediated through the CAMP or Ca⁺² signal transduction pathway, but might occur through non-receptor – mediated mechanisms [27]. Vitamin U is effective against chronic gastric ulceration in the rat with sulfhydryl containing agents has been studied by Salim [28].

[B] DNA / RNA: The effect of vitamin U, a methyl group donor, on enzymatic methylation of DNA in E.coli MRE 600 cells was studied by Lebenka et al. It was found that vitamin U can be used as a donor of methyl groups during bacterial DNA methylation in vivo without changing the specificity of DNA methylation [29]. The tRNA methylation enzymes isolated from E.coli 113-3 grown in a medium with methionine or vitamin U differed in the activity of transfer of the 14CH₃ group from 14CH₃ -S- adenosyl - L-methionine (SAM) to tRNA in the in vitro experiments in heterological systems consisting of tRNA methyltransferases from E. coli 113-3 and a substrate of methylation, Viz. methyl deficient tRNA isolated from E. coli K12W6 [30]. Lebenka et al. suggested that all the types of RNA of E. coli grown in the mineral medium containing vitamin U showed an increased ratio of m2G as compared with the corresponding types of RNA of E. coli after its cultivation in the methionine containing mineral medium [31]. Kocsis et al. indicates that the vitamin U cycle contributes to regulation of S-adenosyl methionine levels rather than preventing depletion of free Methionine [32]. Neuhierl et al. suggested that vitamin U was shown to be the physiological methyl group donor for the Astragalus (Fabaceae) bisulcatus selenocysteine methyltransferase. A model system was set up in E. coli which demonstrated that expression of the plant and although to a much lesser degree, of the bacterial methyltransferase gene increases selenium tolerance and strongly reduces unspecific selenium incorporation into proteins, provided that vitamin U is present in the medium. It is postulated that the selenocysteine methyltransferase under selective pressure developed from a vitamin U dependent thiol / selenol methyltransferase [33]. Lebenka et al. studied the effect of vitamin U on the rate of 14C-uridine incorporation into various categories of RNA in E. coli MRE-600 cells. Vitamin U stimulates the formation of various categories of RNA and causes a quantitative increase in the RNA temperature fraction [34].

[C] Metabolism: Ranocha et al. indicates that the vitamin U cycle consumes half the AdoMet (S-adenosylmethionine) produced, and suggests that the cycle serves to stop accumulation of AdoMet, rather than to prevent depletion of free Methionine. Because plants lack the negative feedback loops that regulate S-adenosylmethionine pool size in other eukaryotes, the vitamin U cycle may be the main mechanisms whereby plants achieve short-term control of AdoMet level [35]. Bourgis et al indicate that vitamin U has a previously unrecognized but often major role in sulfur transport in flowering plants and that evolution of vitamin U synthesis in this group involved a gene fusion event. The resulting bipartite enzyme is unlike any other known as methyltransferase [36]. The physiological roles of the YkfD (a gene) and YagD (Escherichia Coli possesses a protein) products appear to reside in the acquisition of vitamin U, which is an abundant plant product, and its utilization for methionine biosynthesis [37]. Matsuo et al. studied a pharmacological difference between vitamin U and methionine (Met) at higher dose was tested on the fatty liver in choline-deficient rats. Vitamin U normalized the fatty liver. In contrast, Methionine accelerated the syndrome accompanying with increased liver weight [38].

[D] Bio Cholesterol: Nakamura et al. studied the effect of L-form vitamin U in 26 patients with hypercholesterolemia during the oral administration period for 8 weeks. The oral administration of vitamin U resulted in the statistically significant decrease of serum total cholesterol but not of serum triglycerides [39].

Vitamin U markedly increased the fecal excretion of both 14C-bile acids and 14C-neutral sterols in 14C-cholesterol injected mice, and did not inhibit both intestinal absorption of 14C-cholesterol and biosynthesis of 14C-cholesterol from 14C-acetate in mice [40]. Vitamin U dose-dependently lowered the increased plasma LDL and normalized the decreased HDL in dietary – induced hyperlipidemic rats [41]. The conversion rate from 14C-cholesterol to its 7-alpha-hydroxylated metabolites was studied in the microsome system prepared from mice liver with the pretreatment of vitamin U. In results, the increased amounts of 7-alpha-hydroxylated metabolites by vitamin U show a possible activate ion cholesterol 7-alpha-hydroxylase [42].

[E] Biosynthesis: A continuous flow procedure has been developed by Davis et al. for the synthesis of 11C-methyl iodide and L-(S-methyl-11C) methionine from $11CO_2$ [43]. Methionine-192 forms a part of the binding crevice of alpha-chymotrypsin. The aim of this investigation was to find a nucleophile that would displace a methyl group from the sulfonium cation of [S-(13C) methylmehionine-192]-alpha-chymotrypsin without disrupting the five disulfide bridges of the protein , thereby producing [(epsilon-13C) methionine-192]-alpha-chymotrypsin , an isotopically enriched version of the native enzyme desirable for 13C NMR this was studied by Matta et al. [44]. Homolog of the Sam4 and Mht 1 proteins exist in other eukaryotes, indicating that such enzymes would be universal and not restricted to the bacterial or fungal kingdoms. New pathways for AdoMet or vitamin U-dependent methionine synthesis are presented by Thomas et al. [45].

General

Vitamin U a known stimulator of the methylation reaction, was studied by Blium et al. The experiments conducted have shown that the methylation processes in all the studied tissues (heart, liver, small intestine mucosa, thymus and spleen) depend on the quaterin and the vitamin U effect [46]. A study by Gessler and Bezzubov showed that vitamin U is rapidly absorbed in body and accumulates in liver and kidneys of men and rates [47]. The antiphlogistic effect of vitamin U comes in conjunction with its ability to exercise a protective action against lesion of the gastric mucosa produced by acetyl-salicylic acid [48]. Trossat et al. suggested that about 40% of the vitamin U was located in the cholesterol in unsalinized W. biflora plants, as was about 80% in salinized plants; the chloroplastic pool in both cases was approximately 0-1 mumol mg-1 chl. In contrast,> or = 85% of the vitamin U was extrachloroplastic in pea (pisum sativum L.) and spinach (spinacia oleracea L.) which lack 3'-dimethylsulfoniopropionate (DMSP). DMSP synthesis may be associated with enchanced accumulation of vitamin U in the chloroplasm [49]. Vitamin U was found to be an intermediate in the biosynthesis of DMSP-amine in Spartina-alternifloral [50]. Vitamin U had moderate radioprotective activity, the efficiency of radioprotection was 15-30%, the value of dose decrease coefficient-1.2. Biological effect of vitamin U was probably provided by its ability to decrease the level of lipid peroxidation and inhibit monoamine oxidase activity [51]. The importance of methyl group storage in vitamin U is shown by comparison with choline and choline phosphate pools [52]. Vitamin U and S-adenosylmethionine in plant tissue studied by a dansylation, dual-isotope method analysis by Macnicol [53].

Complexes of Vitamin U

Vitamin-U, an alpha-amino acid having ionic chlorine has certain profound bio medical significance. There is a definite role of vitamin U in occurrence and treatment of certain digestive system diseases like gastric ulcer, duodenal ulcer, hyperlipidemia etc. Application of vitamin U for several other diseases is also being studied to a significant level. Metabolism, biosynthesis, other applications of vitamin U are also being studied by various research teams. In the bio-inorganic field complexes of vitamin U in binary and ternary forms are also being studied for their stability, structure and biomedical applications. However, the study of vitamin-U biochemistry is still an emerging field and a lot more is expected to come out in a few decades.

Lipids per oxidation interaction reactions of vitamin U with nickel are reported in animals [54]. Synthesis and spectral characterization of Cu (II) with vitamin U and other ligands was carried out by Akbarov team [55]. Mono dentate N-bonded amino acids and vitamin U mixed-ligand complexes of some 3d metal chlorides have been studied [56]. The mechanism of formation of isomeric complexes of Cu (II), Co (II), and Zn (II) with alpha - amino acid has been suggested [57]. The use of Co (III) complexes with vitamin U and glutamic acid in treatment of hepatitis was carried out using spectrophotometry [58]. The pharmaceutical compounds containing dimethylsulfoxide and vitamin U are also considered for treatment of physiological and mental treatment of physiological and mental health problems [59]. Formation of 1:1:1 ternary complex species [MAL] has been inferred and the relevant equilibrium has been established from pH measurements on the interaction of M³⁺ ions (M = La³⁺, Pr, Sm, Gd) with ligand A [HA=oxine] in the presence of the ligand L [HL=vitamin U] in aqueous medium at ionic strength of 0.2 and at varying temperatures 25 °C & 35 °C [60].

Table I. Analytical Data and Some Physical Properties of the Metal Chelates^a.

Compound Molecular	Molar Conductance ohm ⁻¹ Cm ² mol ⁻¹	Color	Formula Weight	Yield % (g)	Analysis (%) Found (Calculated)						D.P.b
					M	С	Н	N	S	Cl	°C
[CrALClO ₄]·H ₂ O C ₁₅ H ₂₁ N ₂ O ₈ Cl ₂ SCr	02.01	Green	512.36	14.60 (00.56)	10.06 (10.15)	35.08 (35.13)	04.07 (04.10)	05.42 (05.46)	06.20 (06.25)	13.81 (13.86)	>300
[CoAL]·2H ₂ O C ₁₅ H ₂₃ CoClN ₂ O ₅ S	01.87	Middle Buff	437.79	14.68 (00.48)	13.44 (13.46)	41.10 (41.16)	05.15 (05.25)	06.24 (06.40)	07.27 (07.31)	08.06 (08.11)	>300
[NiAL]·2H ₂ O C ₁₅ H ₂₃ ClN ₂ NiO ₅ S	01.89	Parrot	437.55	15.70 (00.52)	13.38 (13.41)	41.07 (41.14)	05.17 (05.26)	06.20 (06.40)	07.28 (07.31)	08.05 (08.11)	>300
[CuAL]·2H ₂ O C ₁₅ H ₂₃ CuClN ₂ O ₅ S	01.98	Yellowish Green	442.41	15.93 (00.53)	14.04 (14.36)	40.43 (40.69)	05.05 (05.20)	06.13 (06.33)	07.18 (07.23)	07.98 (08.02)	>300

 a_A =oxine anion; L=vitamin U anion; bdecomposition point.

CONCLUSION

Vitamin U is a recently understood and important biomolecule having ionic structure with an alpha-amino acid end group. Biochemical importance of this compound is being understood now with significant research work being carried out by various terms. This presumed vitamin has noteworthy impact on gastro intestinal track and some other beneficial effects too. This molecule also easily forms complexes with various metal ions. Some unique properties of this molecule will lead to exciting bio chemical applications in future.

REFERENCES

- [1] K.Sakamoto, A.Inoue, M. Nakatani, H. Kozuka, H. Ohta and Y. Osajima. *Biosci Biotechnol Biochem.***1996** Sep.60(9),1486-7.
- [2] A.A. Bezzubov & N.N. Gessler, Prikl Biokhim Mikrobiol. 1977 Mar-Apr,13(2),301-9.
- [3] G.N. Khuchua & A.B. Stasiak, *Prikl Biokhim Mikrobiol.* 1975 Nov-Dec, 11(6),914-21.
- [4] C.P. Leung, W.K. Leung, J.chromatogr. 1989 Oct 6, 479(2),361-7.
- [5] S. Uehara, S. Nojiri, M. Takahashi & Y. Watanabe, Yakugaku Zasshi. 1994 Sep, 114(9), 697-703.
- [6] K. Seri , T Matsuo , Taniguchi T, Amemiya K, Kudo M, saito G, M Asano , T. Kato. *Arzneimittelforschung*. **1978**, 28(10),1711-2.
- [7] G. Cheney, Calif. Med. 1949, 70, 10.
- [8] G. Cheney, Mil. Surgeon. **1944**, 95, 446-454.
- [9] V.J. Gianelli and V.Bellafiore, Med. Clin.North America, 1945, 29, 706-713.
- [10] G.Cheney, Calif Med. 1952,77(4), 248-52.
- [11] G.Cheney, Am. J Gastroenterol. 1954 Mar, 21(3), 230-50.
- [12] G.Cheney, Stanford Med Bull. 1955 May, 13(2), 204-14.
- [13] G. Cheney, SH Waxler and IJ. Miller, Calif. Med. 1956 Jan, 84(1), 39-42.
- [14] GV Stoliarov, Mys Ko, Zh Nevropatol Psikhiatr Im SS Korsakova, 1981,81(8),1209-12.
- [15] WE Roediger, W. Babidge and S. Millard, Gut. 1996 Jul, 39(1), 77-81.
- [16] LIa Areshkina, EP Skorobogatova, VN Bukin, Prikl Biokhim Mikrobiol, 1979 Jan-Feb, 15(1), 12-7 (1979).
- [17] S Ko, AC Eliot and JF Kirsch, Arch Biochem Biochem Biophys. 2004 Jan1, 421(1) 85-90.
- [18] J. Kim, M. Lee, R. Chalam, MN Martin, T Leustek and W. Boerjan, *Plant Physiol*, **2002** Jan, 128(1), 95-107.
- [19] K. Seri, K. Amemiya, H. Sugimoto, and T. Kato. Arzneimittelforschung. 1979, 29(10),1517-20.
- [20] Al Lebenka, LA Rachkus and SL Kanopkacite, Vopr Med Khim, 1981 Mar-Apr, 27(2), 207-10.
- [21] NN Gessler, AA Bezzubov, EV Podlepa and VL Bykhovskii, *Prikl Biokhim Mikrobiol* **1991** May-Jun,27(3), 358-64
- [22] Simon Martin, Bio Med New Sletter. 1995 May, Issue 11.
- [23] T.Watanabe, S.Ohara, T.Ichikawa, K.Saigenji and K. Hotta, Dig Dis Sci. 1996 Jan, 41(1), 49-54.
- [24] T. Watanabe, S. Ohara, S. Miyazawa, K. Saigenji, and K. Hotta, J. Gastroenterol Hepatol, 2000 Jan, 15(1), 45-52.
- [25] AS Salim, J. Pharm Sci. 1992 Jul, 81(7), 698-700.
- [26] Alu Lebenka, SI Kanopkaite and Ial Burianov, Biokhimiia. 1981 Dec, 46(12), 2160-3.
- [27] Alu Lebenka and SI Kanopkaite, Mikrobiologiia, 1980 May-Jun, 49 (3), 440-4.
- [28] AIu Lebenka, IuA Rachkus and SI Kanopkaite, Prikl Biokhim Mikrobiol, 1979 Sep-Oct, 15(5), 693-8.
- [29] MG Kocsis, P Ranocha, DA Gage, ES Simon, DRhodes, GJ Peel, S Mellema, K Saito, M Awazuhara, C Li, RB Meeley, MC Tarczynski, C Wagner and AD Hanson. *Plant Physiol.* **2003** Apr,131(4), 1808-15.
- [30] B. Neuhierl, M. Thanbichler, F. Lottspeich, A. Block, J. Biol Chem. 1999 Feb-26,274(9), 5407-14.
- [31] Alu Lebenka, IuA Rachkus & SI Kanopkaite, Ukr Biokhim Zh. 1981-Oct, 53(5), 64-8.
- [32] P. Ranocha, SD McNeil, MJ Ziemak, C Li, MC Tarczynski and AD Hanson. Plant J.2001 Mar, 25(5),575-84.
- [33] F. Bourgis, S Roje, ML Nuccio, DB Fisher, MC Tarczynski, C Li, C Herschbach, H Rennenberg, MJ Pimenta, TL Shen, DA Gage and AD Hanson. *Plant Cell*. 1999 Aug, 11(8), 1485-98.
- [34] M Thanbichler, B Neuhierl and A Bock, J. Bacteriol. 1999 Jan, 181(2), 662-5.
- [35] T. Matsuo, K Seri & T Kato, Arzneimittelforschung. 1980, 30(1), 68-9.
- [36] N. Nakamura, H. Vzawa, K. Kanazawa, Y. Tamai, Y. Tashiro and M. Koide. *Arzneimittelforschung* **1981**, 31(4), 725-9.
- [37] K. Seri, T. Matsuo, M Asano, R. Sato & T. Koto, Arzneimittelforschung. 1979, 29(12), 1857-8.
- [38] K. Seri, R. Sato, K. Yasuda and T. Kato. Arzneimittelforschung. 1979, 29(11), 1722-3.
- [39] T. Matsuo, K. Seri and T. Kato. Arzneimittelforschung. 1980, 30(2), 258-9.
- [40] J. Davis, Y Yano, J. Cahoon, and TF Budinger. Int. J Appl Radiat Isot. 1982 May, 33(5), 363-9.
- [41] MS Matta, PA Henderson and TB Patrick. J. Biol Chem. 1981 May 10,256(9),4172-4.
- [42] D Thomas, A Becker, and Y Surdin-Kerjan, J. Biol Chem. 2000 Dec 29, 275(52), 40718-24.

- [43] IaB Blium, IIa Kalvin'sh, NE Kucherenko and EIa Lukevits. Ukr Biokhim Zh. 1987 Sep-Oct, 59(5), 18-24.
- [44] NN Gessler and AA Bezzubov, Farmakol Toksikol. 1987 Jul-Aug; 50(4), 49-51.
- [45] LG Urazaeva, Farmakol Toksikol. 1976 May-Jun, 39(3), 316-9.
- [46] C. Trossat, B. Rathinasabapathi, EA Weretilnyk, TL Shen, ZH Huang, DA Gage and AD Hanson. *Plant Physiol.* **1998** Jan,116(1), 165-71.
- [47] MG Kocsis, KD Nolte, D Rhodes, TL Shen, DA Gage and AD Hanson. *Plant Physiol.* 1998 May, 117(1), 273-81.
- [48] NN Gessler, LI Kharchenko, TE Pavlovskaia and VIa Bykhovskii, *Prikl Biokhim Mikrobiol.* **1996** Nov-Dec, 32(6), 666-8.
- [49] F Menegus, I Lilliu, I Brambilla, M Bonfa and L Scaglioni J. Plant Physiol. 2004 Jan,161(6), 725-32.
- [50] PK Macnicol, Anal Biochem. 1986 Oct, 158(1), 93-7.
- [51] Karimova, Dokl. Akad Nauk. Resp. Uzb.1996,12, 57-59.
- [52] M.M. Akbarov, A.B; Kadyrov, M.A; Mutalibov, A.S; Shadmanov, K.K; Sanayev, B.S. *Uzb. Khim. Zh.***1995**, **5(6)**, 22-26.
- [53] A.B Akbarov, A.S Mutalibov, "Synthesis and Study of Coordination Compounds of Some 3d Elements With vitamin U and some Alpha-Amino Acids (USSR)." *Deposited Doc.* **1984**, **13** pp
- [54] K.K Khakimov, A.B. Akbarov, "Mechanism of the Formation of Isomeric Compounds of Divalent 3d ions with Alpha-amino acids (USSR)." *Deposited Doc.* **1984**, **9**, 940-984.
- [55] K.K.Shadmanov, E.A. Yurkovskaya, G.A. Gushenko, A.K Sharipov,; A.B. Akbarov, *Uzb. Khim. Zh.* **1992**; 3(4), 468.
- [56] Salim; A.S Mustafa. PTC Int. Appl. Wo 1994, 05, 280.
- [57] J.D.Joshi, Jabali J. Vora, Sangita Sharma, Asha D.Patel, L.S.Bhutadiya. J.Indian Chem. Soc. 2006, 83,78-79.