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SYNTHESIS AND SPECTROSCOPIC INVESTIGATIONS OF Au(III) SELENO-ORGANIC COMPLEXES

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ABSTRACT. Heterocyclic pyridazine continues to attract great interest, mainly arising from a large variety of interesting pharmacological activities, herbicides, insecticides, and fungicides. On the other hand, the current interest in selenium-containing heterocycles is a result of their chemical properties and biological activities. In addition to the many recent publications dealing with the pharmacological potential of a selenium compound, new active formulations are an attractive target for chemical research. 2-((3-cyano-4,6-dimethylpyridin-2-yl)selanyl) acetic acid (pyd-Se), 2-((4-cyano-5,6-diphenylpyridazin-3-yl)selanyl)acetic acid (pydz-Se) and 2-((4,6-dimethyl quinolin-2-yl)selanyl)acetic acid (quin-Se) reacts with gold(III) chloride to produce metal ion complexes of specific composition. These synthesized complexes were characterized by elemental analyses, molar conductivity, FTIR, ^{1}H NMR and transmission electron microscopy (TEM) investigations. The complexes were found to have the formulas $[Au(pyd\text{-}Se)_2]Cl$, $[Au(pydz\text{-}Se)_2]Cl$ and $Au(quin\text{-}Se)_2]Cl$, respectively.

KEY WORDS: Au(III), Organoselenium, Complexation, FTIR, ^{1}H NMR, TEM

INTRODUCTION

The role of the metal ion is important in the field of biology that leads to the improvement of therapeutic efficacy [1, 2]. Selenium is a non-metallic element with enzymatic and chemopreventive roles in cancer [3, 4]. The mineral selenium is a very potent and well-established dietary requirement for both humans and animals [5]. Heterocyclic selenium compounds have a much higher bioavailability than selenium as an inorganic adduct [6]. Organic selenium compounds are generally less toxic than inorganic ones [7, 8]. In the literature there are a lot of papers focusing on the development of organic selenium compounds that have therapeutic efficacy towards some human diseases [9-11]. Mills first discovered glutathione peroxidase in animal tissues in 1957 [12]. Glutathione peroxidase (GPx) contains four identical protein subunits that each contain a selenium (Se) atom in its active site. There are at least four types of Se containing glutathione peroxidase: cytosolic GPx, gastrointestinal (GI) GPx, plasma GPx and phospholipid hydroperoxide GPx. All of the above shows similarities in their structures. Finally, Floh *et al.* reported that GPx are selenozymes that contain selenium in the active site of GPx, and act as an antioxidant by catalyzing hydrogen peroxide reduction [13]. In humans, supplemental levels of 200 µg selenium/day have been reported to exhibit carcinogenic activity, which is 2-3 times the amount of normal dietary levels. All inorganic selenium compounds that express oncogenic activity against cancer cells in vivo do so by interacting with thiol compounds and generating free radical species [14]. The antitumor activity of an organic selenium complex was initiated with dietary *p*-methoxybenzeneselenol, a synthetic organic selenium compound that was found to inhibit azoxymethane-induced hepatic proliferation in female F344 mice without signs of clinical toxicity [15] and was a potent inhibitor of benzo(α)pyrene - jungle stomach tumors in mice [16] and colon carcinogenesis in mice [17]. Later, Reddy *et al.* The chemopreventive effect of 1,4-phenylnibis(methylene)selenocyanate (*p*-XSC) on azoxymethane-induced colon tumor [18, 19], and 7,12-dimethylbenz(α) anthracene-induced breast tumors has been reported during

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the initiation phase of carcinogenesis in mice [20]. Rao *et al.* showed that *p*-phenylenebis (methylene) selenocyanate [21] was a superior cancer chemopreventive agent and less toxic than selenite or natural seleniumamino acid. It was also more effective against colon cancer when taken during the post-initiation phase and inhibits cyclooxygenase activity. Das *et al.* note the inhibitors of 7,12-dimethylbenz(alpha) anthracene (DMBA)/two-stage carcinogenesis of croton oil-induced mouse skin by diphenylmethylsilenocyanate due to thiobarbituric acid inhibition reduced papilla formation during chemically induced carcinogenesis [22]. Several organic selenium compounds have been synthesized and studied for their antimicrobial activity [23, 24]. The most potent is epicillin (2-phenyl-1,2-benzisosilinazole-3(2H)-one), which possesses anti-inflammatory, cytosclerotic and antimicrobial activity against *S. aureus* [25]. Carboxylates are a very important class of ligands in bioorganic chemistry. This can be adopted for the versatility of the RCOO- ligand and the wide range of coordination modes it can adopt. Many carboxylate complexes have been characterized and the coordination chemistry of carboxylic acids has been well documented [26]. In metal-carboxylate complexes, positive metal centers (Mn+) combine with anionic carboxylate groups (RCOO-). The bonding can range from ionic to polar covalent with physical and chemical properties dependent on the nature of the R group [26]. Here we report the results of our studies on chelating properties and characterization of gold(III) complexes of 2-((3-cyano-4,6-dimethylpyridin-2-yl)selanyl)acetic acid (pyd-Se), 2-((4-cyano-)5,6-diphenylpyridazin-3-yl)selanyl)acetic acid (pydz-Se) and 2-((4,6-dimethylquinolin-2-yl)selanyl)acetic acid (quin-Se).

EXPERIMENTAL

Synthesis of gold(III) organoselenium complexes

The new chelates 2-((3-cyano-4,6-dimethylpyridin-2-yl)selanyl)acetic acid (pyd-Se), 2-((4-cyano-5,6-diphenylpyridazin-3-yl)selanyl) were done. Prepare acetic acid (pydz-Se) and 2-((4,6-dimethylquinolin-2-yl)selanyl) acetic acid (quin-Se) by methods reported elsewhere [27] (Figure 1). These compounds were recrystallized from ethanol and the spectral characteristics were compared with the reported data. The ligands pyd-Se, pydz-Se and quin-Se (2 mmol, 539, 789 and 589 mg, respectively) were dissolved in methanol (30 ml) and for this $AuCl_3$ (1.0 mmol) was dissolved in methanol (30 ml) Add slowly with continuous stirring over 45 minutes, then adjust the pH of the solution to 7-8 using a 5% alcohol ammonia solution. The reaction mixture was remixed for 3 hours. The obtained greenish-brown solid complexes were collected on a filtrate and washed with cold methanol and then with diethyl ether. The complexes were dried over anhydrous calcium chloride in a vacuum desiccator. The yields of the isolated gold complexes were in the range of 65-70%.

Instruments

Carbon, hydrogen, and nitrogen analyzes were performed in a Vario EL Fab. CHNS. The infrared spectra were recorded on a Bruker infrared spectrometer in the range of 400–4000 cm^{-1}. The 10^{-3} molar conductivity in DMSO solvent was measured on a HACH conductivity scale model. Measurements were taken at room temperature for fresh solutions. ^{1}H-NMR and ^{13}C-NMR were recorded as DMSO solutions on a 600 MHz Bruker spectrometer using TMS as an internal standard. Transmission electron microscopy images were performed using a JEOL 100s microscope.

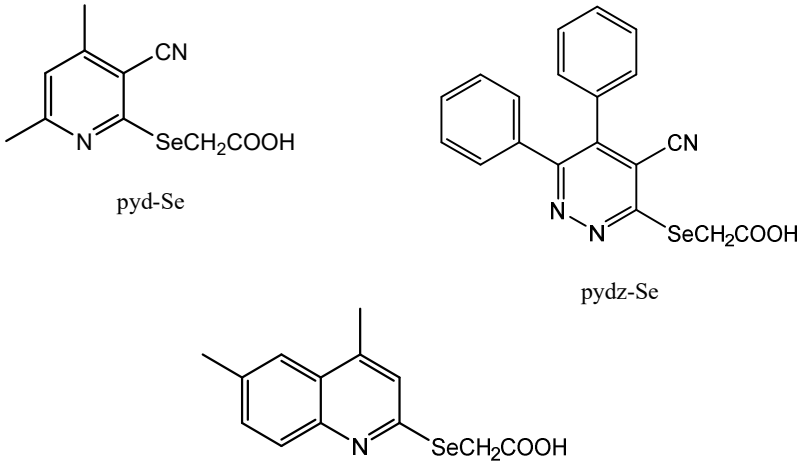

Figure 1. Structures of the synthesized organoselenium substituted compounds.

RESULTS AND DISCUSSION

Microanalytical and molar conductance data

Organic selenium complexes were prepared by heating methanol solutions together of the appropriate ligand and gold(III) chloride. All synthesized complexes are hygroscopic and stable at room temperature. Gold(III) complexes of pyd-Se, pydz-Se and quin-Se are insoluble in methanol, ethanol and benzene, but soluble in DMSO and DMF. The characterization data are shown in Table 1. The molar conductivity values of the pyd-Se, pydz-Se and quin-Se complexes (10^{-3} M solution in DMSO) were found to be in the range 56-71 $\Omega^{-1}.cm^2.mol^{-1}$ at 25 °C. These slightly higher values indicate that the complexes are ionic [28]. These data are consistent with the elemental analysis calculated that one of the chloride ions was present outside the coordination domain, then verified by adding a solution of $AgNO_3$ to solutions of synthetic gold(III) complexes dissolved in nitric acid.

Table 1. Characteristic data of the gold(III) organoselenium complexes.

Complexes	Mwt g/mol	Elemental analysis % found (calcd.)				Yield %	Λ_M $\Omega^{-1}.cm^2.mol^{-1}$
		C	H	N	Au		
[Au(pyd-Se)$_2$]Cl	768.75	31.19 (31.25)	2.30 (2.36)	7.08 (7.29)	25.21 (25.62)	68	71
[Au(pydz-Se)$_2$]Cl	1019.01	44.34 (44.79)	2.34 (2.37)	8.11 (8.25)	19.06 (19.33)	65	67
[Au(quin-Se)$_2$]Cl	818.85	38.09 (38.14)	2.87 (2.95)	3.40 (3.42)	23.89 (24.05)	70	56

Mass spectra

The ligands pyd-Se, pydz-Se, and quin-Se show their highest mass peaks at m/z 269, 394, and 294, respectively, corresponding to M^++1, M^+, and M^++2 ions. Prominent portions of the spectra

correspond to The mass for all pyd-Se, pydz-Se, and quin-Se complexes with $[Au(pyd\text{-}Se)_2]Cl$, $[Au(pydz\text{-}Se)_2]Cl$, and $[Au(quin\text{-}Se)_2]Cl$ ions, on respectively. Moreover, the coordination of organic selenium bonds with gold metal ions is confirmed by the appearance of the corresponding moieties of $[Au(pyd\text{-}Se)_2]$, $[Au(pydz\text{-}Se)_2]$ and $[Au(quin\text{-}Se)_2]$. The presence of lower mass fragments that also appeared in the ligand spectra confirms the presence of gold metal ions. The analytical data presented in Table 1 confirm the formulas of the three ligand complexes as $[Au(pyd\text{-}Se)_2]Cl$, $[Au(pydz\text{-}Se)_2]Cl$ and $[Au(quin\text{-}Se)_2]Cl$ [27].

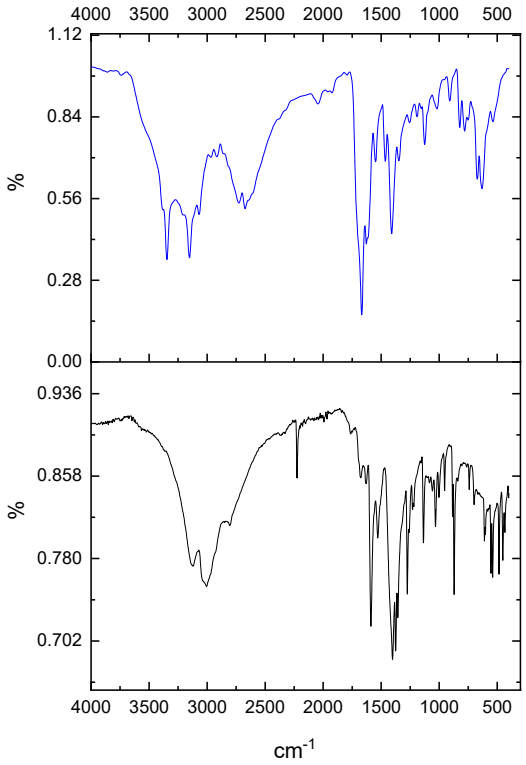

Figure 2a. FT IR spectra of pyd-Se (black) and $[Au(pyd\text{-}Se)_2]Cl$ complex (blue).

Infrared spectra

The FTIR spectra of ligands pyd-Se, pydz-Se and quin-Se show characteristic absorptions at pyd-Se: ν_{max} (cm^{-1}) 3410 (O-H), 3050 (CH-aromatic), 2200 (C≡N),1730 (C=O), 1600 (C=C-aromatic); pydz-Se: ν_{max} (cm^{-1}) 3405 (O-H), 3050 (CH-aromatic), 2200 (C≡N),1740 (C=O), 1600 (C=C-aromatic) and quin-Se: ν_{max} (cm^{-1}) 3400 (O-H), 3050 (CH-aromatic), 1720 (C=O), 1600 (C=C-aromatic).The infrared spectra of complexes of gold(III), $[Au(pyd\text{-}Se)_2]Cl$, $[Au(pyd\text{-}Se)_2]Cl$ and $[Au(quin\text{-}Se)_2]Cl$, in a KBr discs are shown in the Figure 2 and its scope assignments.In the infrared spectra of the free bonds pyd-Se, pydz-Se and quin-Se, the extended vibration spectral bands of the OH group and C=O (COOH) group are located at about 3400–3410 and 1720–1740 cm^{-1}, respectively. These bands are absent if the gold(III) complex is present indicating the participation of the carboxyl group in the coordination domain, which is

discussed when the proton of COOH group is removed. The intensities of the ν(C≡N) and ν(C=C) bands are shifted towards lower wavenumbers compared to the spectra of free organic selenium ligands and appear in the range 2041–2050 cm^{-1} and 1620–1650 cm^{-1} [29], this result proves that aromatic ring and quionline ring are affected under complexation. Gold(III) complexes have two distinct bands at 1456–1579 cm^{-1} and 1290-1414 cm^{-1}, due to ν_{as}(COO) and ν_{s}(COO), respectively. The carboxylic group can be coordinated with metal ions in three forms, so we can learn about the binding geometry of the carboxylate ligand. Deacon and Phillips [36] studied the criteria that can be used to distinguish between the three binding states of carboxylate complexes. The energy separation between ν_{asym}(COO) and ν_{sym}(COO) was found to be <200 cm^{-1} (141–189 cm^{-1}), and this indicates the bi-dentate nature of the carboxylate ion [30], because in the case of binary coordination, it has been reported For that energy separation is less than 200 cm^{-1}. Moreover, the infrared spectra of the complexes show two new bands in the far infrared region at 458–530 cm^{-1}. These absorbances can be assigned to ν(M-O) [29].

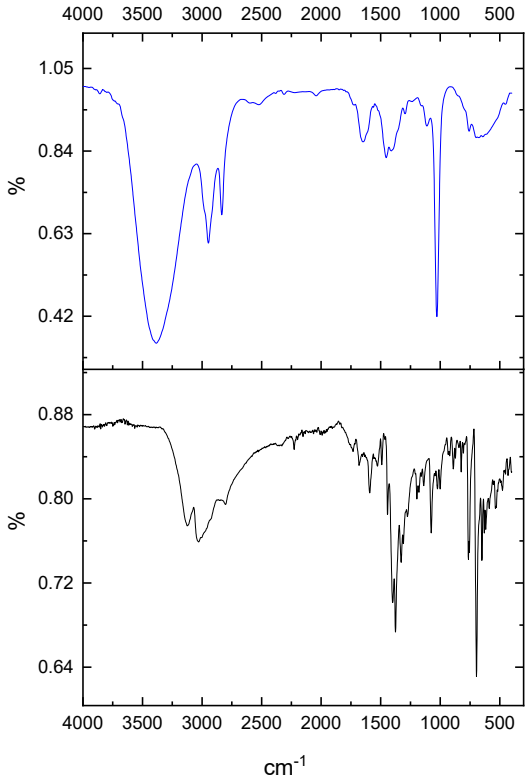

Figure 2b. FT IR spectra of pydz-Se (black) and [Au(pydz-Se)$_2$]Cl complex (blue).

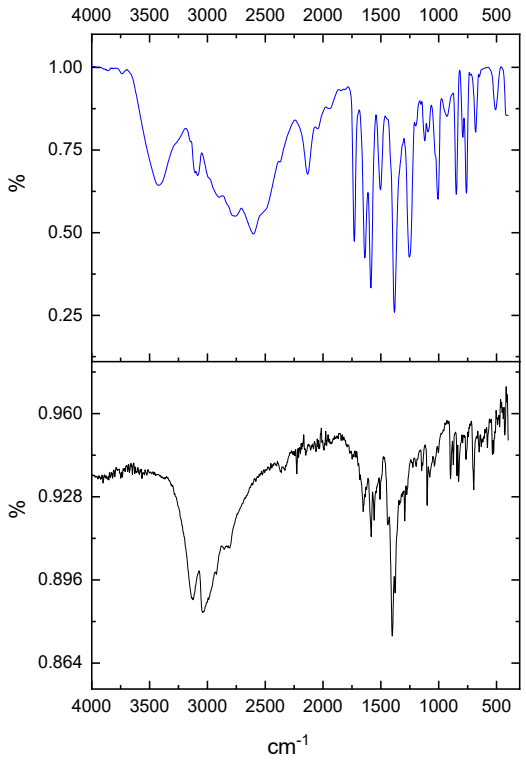

Figure 2c. FT IR spectra of quin-Se (black) and $[Au(quin\text{-}Se)_2]Cl$ complex (blue).

^{1}H-NMR spectra

^{1}H-NMR spectrum of pyd-Se: DMSO-d_6 (δ, ppm) = 7.43 (s, 1H, CH –pyridine), 3.32 (s, 2H, $SeCH_2$), 2.48 (s, 3H, (CH_3), 2.47 (s, 3H, CH_3), and the disappeared of COOH because of H-bond [27]. ^{1}H-NMR spectrum of pydz-Se: DMSO-d_6 (δ, ppm) = 14.15 (s, 1H, COOH), 7.43-7.29 (m, 10H, Ar-H), 3.36 (s, 2H, $SeCH_2$) [27]. ^{1}H-NMR spectrum of quin-Se: DMSO-d_6 (δ, ppm) = 11.53 (s,1H, COOH), 7.82-7.38 (m, 4H, CH–quinoline), 3.40 (s, 2H, $SeCH_2$), 2.62 (s, 3H, CH_3), 2.51 (s, 3H, (CH_3) [27].

^{13}C NMR spectra

^{13}C-NMR spectrum of pyd-Se: ($CDCl_3$, 75 MHz) δ 20.58-24.53 $(CH_3)_2$, 29.70 (CH_2), 108 (C-CN), 114 (CN), 122 (H-C), 151-152 (C- CH_3), 155 (C-Se), 162 (COOH) [27]. ^{13}C-NMR spectrum of pydz-Se: ($CDCl_3$, 75 MHz) δ 56 (CH_2), 112 (C-CN), 121 (CN), 127.78-128.94 $(Ph)_2$, 130 (Ph-C-C), 136 (Ph-C- N), 161 (C-Se), 172 (COOH) [27]. ^{13}C-NMR spectrum of quin-Se: ($CDCl_3$, 75 MHz) δ 18.6-18.7 $(CH_3)_2$, 21.8 (CH_2), 120 (CH_3-C-Se), 122 (Ph-C-C-Se), 126-147 (Ph), 149 (C-Se), 153 (COOH) [27]. In the spectrum of $[Au(pydz\text{-}Se)_2]Cl$ complex, the signals disappear at δ 14.15 ppm in the pydz-Se ligand, indicating decarboxylation and complex formation. Based on the physico-chemical and spectroscopic studies, the proposed temporary structures for the complexes are shown in Figure 3.

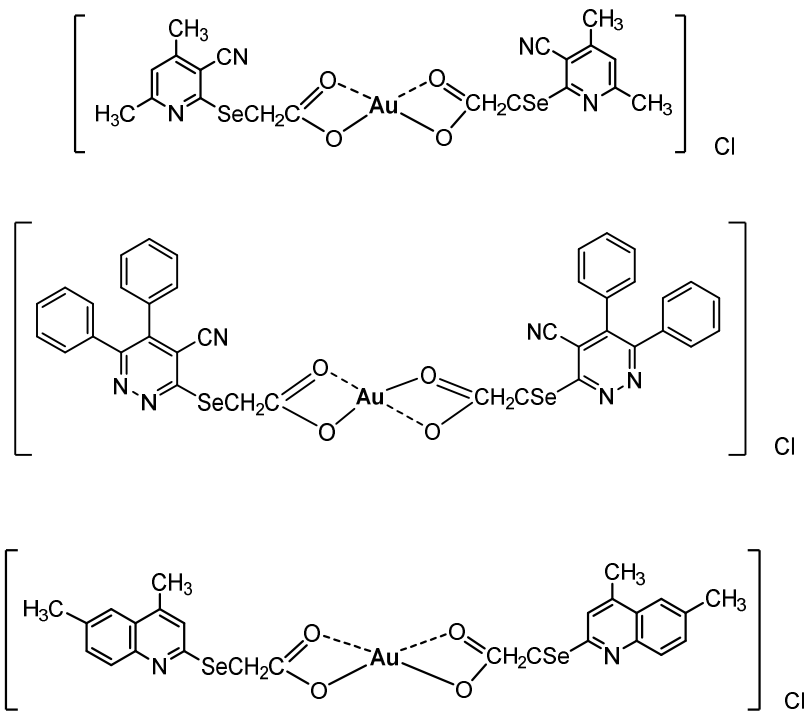

Figure 3. Tentative structures of the gold(III) complexes of pyd-Se, pydz-Se and quin-Se ligands.

Transmission electron microscopy image

The TEM morphology of pure gold(III) complexes is shown in Figure 4. The TEM analysis technique confirmed the presence of nanoscale gold(III) complexes [31–33]. The TEM image showed spherical NPs of gold(III) ions that appeared as dark spots. The diameter of the Au(III) complexes ranges from 10–50 nm.

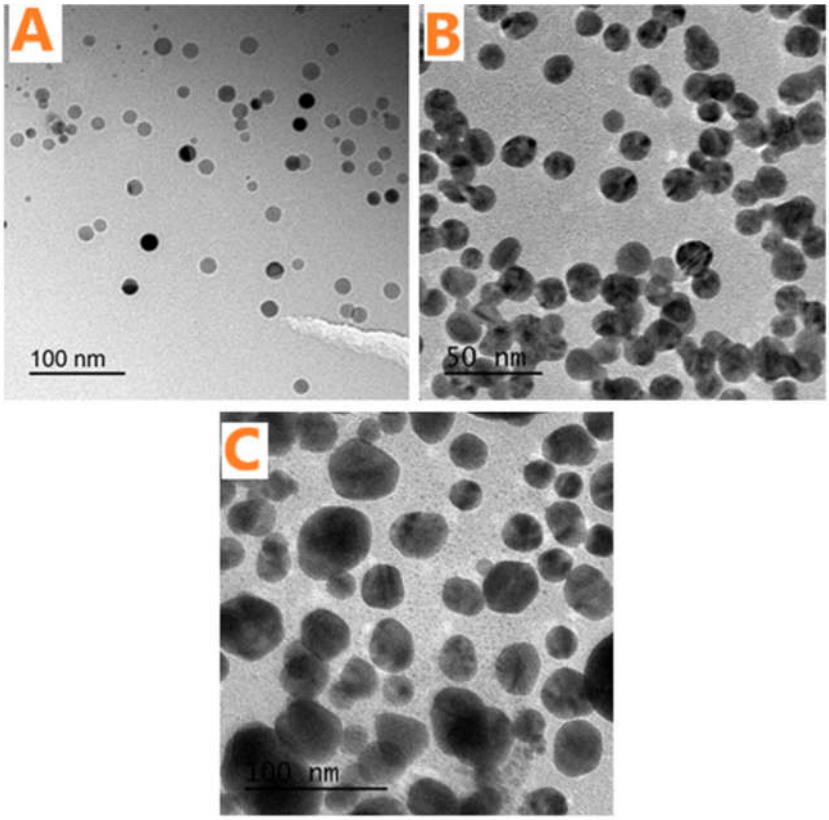

Figure 4. TEM of the gold(III) complexes of A: pyd-Se, B: pydz-Se and C: quin-Se ligands.

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