



Synthesis, Characterization, Antifungal And Diffraction Studies Of Some Transition Metal Ion Complexes Of 2, 2-Diphenyl-2-Hydroxyacetic Acid- 4-Hydroxyphenylalanine

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Abstract

The present work is focused on the synthesis of novel complexes of Mn(II), Fe(III), Co(II), Zn(II), and Cu(II) that arise from the condensation of 2, 2-Diphenyl-2-hydroxyacetic acid with 4-hydroxyphenylalanine. By using FT-IR, UV-Vis, microanalyses, X-ray diffraction analysis, magnetic susceptibility, the ligand and its complexes were characterized and the antibacterial properties have been examined. The results show that the ligand coordinates with the metals in an octahedral shape, acting as a bidentate ligand. Using bacterial and fungal strains, the antibacterial properties of synthesized ligands and metal complexes were studied. According to the results of the study, metal complexes exhibit higher levels of reactivity in comparison to their parent ligand. The XRD analysis demonstrates that the metal complexes are orthorhombic systems that are crystalline in nature.

Keywords:

2,2-Diphenyl-2-hydroxyacetic acid; 4-hydroxyphenylalanine ; XRD; antifungal.

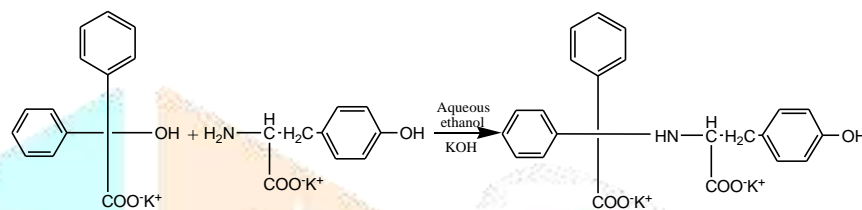
1. Introduction

Coordination compounds have gained a lot of attention lately due to their unique design and useful characteristics. These substances can be used as optical, magnetic, catalytic, luminescent, or electrical substances. A significant part of the pharmaceutical industry is played by amino acids and the compounds they form with various metal ions (1-5). Several investigations have shown that chelation increases the bacteriostatic and carcinostatic properties of physiologically active substances. A few drugs inhibit tumor growth and are more effective when given as metal chelates. Additionally, Schiff base complexes have drawn increased attention due to developments in the field of bioinorganic chemistry because several of these have been demonstrated to be viable models for physiologically relevant species (6–9). Schiff bases and their metal complexes have been extensively studied due to their crucial roles in the main group and the natural transition-metal coordination chemistry resulting from their rapid synthesis and variety of structures.(10-13). In order to synthesize them, primary amines must react via condensation with active carbonyl in the presence of an appropriate solvent. These metal complexes are created by adding the schiff-base ligand, in the right ratio, to a metal precursor under the right experimental settings. There have been numerous documented uses for Schiff bases and related metal complexes. They have been used by researchers as chelating ligands in coordination chemistry (14-16), as catalysts (17-20), as dyes (21,22), as initiators in polymerization (23), and as molecules that emit light (24,25). They have undergone biological testing as insecticides (26-28), antibacterial (29-31), antifungal (32-35), anticancer (36-38), and antiviral (39,40) agents.

2. Experimental

The ligand molecule, HBT was synthesized by the condensation of ethanolic solution of 2,2-Diphenyl-2-hydroxyacetic acid with an ethanolic solution of 4-hydroxyphenylalanine potassium salt and refluxing the mixture for three hours in a water bath, the 2,2-Diphenyl-2-hydroxyacetic acid-4-hydroxyphenylalanine ligand was synthesized and the ligand crystallized out was cleaned with ethanol and then dried on anhydrous CaCl_2 . The melting point was found to be 290°C . The metal complexes were prepared by mixing the heated ethanolic solution of the ligand solution with the metal acetate/chloride solution. The mixture refluxed for an hour and a pinch of sodium acetate trihydrate was added, and then it was allowed to cool. The crystalline

precipitate was collected, washed with water several times, and then dried in a desiccator. Using the KBr disc method, the IR spectra of the ligand and its complexes were measured using the Jasco-FT-IR-4100 model spectrophotometer over the frequency range of 400–4000 cm^{-1} . A UV-VIS spectrophotometer model JascoV-550 was used to measure the DRS UV-visible spectra of the solid complexes. Molar magnetic susceptibilities at room temperature (298 K) were measured by Faraday's method and corrected for diamagnetism using Pascal's constants. The molar conductance of the complexes at a concentration of about 10^{-3} M was measured at 28 ± 2 °C using a Philips conductivity bridge.



Scheme 1. The reaction pathway of the ligand HBT

X-ray diffraction study of the ligand and complexes were studied using an Aeris research benchtop X-ray diffractometer in the range $10-90$ 2θ values. The antifungal activity of the compounds was studied using disc method. The antifungal studies of the ligand and complexes against various fungal strains such as *Penicillium* sp., *Fusarium* sp., *Pythium* sp., *Lasiodiplodia theobromae* and *Aspergillus* sp. were studied using potato dextrose agar medium.

3. Results and discussions

3.1. Characterization of ligand and its metal complexes

Scheme. 1 represents the synthesis of the HBT ligand. A number of analytical and spectroscopic investigations were used to confirm the structure of the newly synthesized ligand and its metal complexes. The structure of the ligand was elucidated using CHN analysis and spectral data. The melting point of the ligand was found to be 290°C . Utilizing micro analytical methods, the percentages of nitrogen, carbon, and hydrogen were determined. All of the compounds had stoichiometry values of 1:1 and 1:2. In this instance, α,α -Diphenyl- α -hydroxyacetic acid -4-hydroxyphenylalanine (HBT)

interacts with the ions of common transition metals by acting as a bidentate ligand. The calculated and measured percentages of carbon, hydrogen, and nitrogen agreed fairly well.

Table 1. Micro analytical, magnetic moment and conductance data of HBT ligand and its transition metal complexes

Compound	Molecular Weight	Melting point	Colour	yield	Ω^{-1}	μ_{eff}	M%
$\text{C}_{23}\text{H}_{19}\text{NO}_5(\text{HBT})$	391.43	290 ⁰	Pale yellow	80		-	-
$\text{Mn}(\text{BT})_2(\text{H}_2\text{O})_2$	873.79	>300 ⁰	Light brown	70	20.55	5.68	6.28 (6.36)
$\text{Fe}(\text{BT})(\text{H}_2\text{O})_2\text{Cl}_2$	554.27	>300 ⁰	Light brown	70	9.73	3.18	10.07 (10.12)
$\text{Co}(\text{BT})(\text{H}_2\text{O})_4$	522.36	>300 ⁰	Pink	60	4.56	4.32	11.28 (11.90)
$\text{Cu}(\text{BT})(\text{CH}_3\text{COO})_4$	690.98	>300 ⁰	Brown	80	17.36	2.18	9.19 (9.28)
$\text{Zn}(\text{BT})(\text{CH}_3\text{COO})_4$	692.81	>300 ⁰	White	70	19.35	DIA	9.17 (8.94)

3.2. Electronic spectra and magnetic moments

The solid state electronic spectrum of the ligand was recorded in the range 200-900 nm and it exhibits bands at 279,342 and 367 nm. The bands are attributed to the $n \rightarrow \pi^*$ and $\pi \rightarrow \pi^*$ transitions respectively. The shift in the value of the bands from the ligand to the complexes explains the coordination that occur between the metal ion and the ligand. The complexes were found to be non-electrolytic based on their molar conductance values in methanol at a concentration of 1×10^{-3} M at $28 \pm 2^\circ\text{C}$. Manganese (II) ion with d^5 configuration is capable of forming spin-free as well as spin-paired complexes but due to the additional

stability of the half-filled d-shell they preferably form spin-free complexes. Mn (II) complexes show low intensity weak bands at 330 nm due to $n \rightarrow \pi^*$ and 419 nm ${}^6A_{1g} \rightarrow {}^4T_{1g}(G)$ which have been assigned to transitions, and respectively, in an octahedral field of Mn (II) ion. In the current case the complex possess a value of 5.68 BM which suggests the octahedral nature of the complex. In the current work absorption band of Fe (III) complex are in the range 282 and 330 nm assigned to $\pi \rightarrow \pi^*$, $n \rightarrow \pi^*$ transition. A strong charge transfer band is observed at 389 nm due to CT transition. From spectral data, an octahedral geometry is proposed for the Fe (III) chelate. Fe (III) complex have a magnetic moment value of 3.18 BM which corresponds to three unpaired electrons which suggest an octahedral geometry. The octahedral Co(II) complexes are pink or reddish brown in color. In the present work Co(II) metal complexes two bands present in electronic spectra of Co(II) at 255, 355 and 345 nm. It is assignable to octahedral geometry. In the present case Co (II) complex has a magnetic moment value of 4.32 BM suggesting their octahedral geometry. The electronic configuration of Cu(II) is d^9 and the ground state being 2D . The ground state of the octahedrally coordinated Cu(II) ion is 2E_g , in tetrahedral field is 2T_2g and for the square planar complexes is ${}^2B_{1g}$. The d^9 configuration undergoes tetragonal distortion because of Jahn-Teller distortion and leads to splitting of the 2E_g and 2T_2g levels in to ${}^2B_{1g}$, ${}^2A_{1g}$ and ${}^2B_{2g}$, 2E_g levels, respectively. The Cu(II) complex electronic spectrum shows a broad band in the region 478-700 nm and is assignable to C-T transition. The magnetic moment value of copper complex is 2.18 BM corresponding to their one unpaired electron suggesting their octahedral geometry. The electronic spectra of Zn(II) complexes is not possible since there is no unpaired electrons and the 'd' sub shell is completely filled. They show charge transfer transitions in the range of 280-350 nm and they are diamagnetic in nature. Most of the complexes are tetrahedral even though some octahedral complexes have also been reported.

3.3. IR spectra of the ligand and its complexes

The characteristic IR spectra of the metal complexes of the spectra are given in Table.2. The IR band in the region $3500-3100\text{ cm}^{-1}$ due to $\nu(\text{OH})$ stretching vibrations in the metal complexes indicating that the presence of water coordinated to the metal which is further supported by the new peaks in the regions

of

750-850 cm^{-1} . The C-O stretch at 1244 cm^{-1} is red shifted to 1170-1200 cm^{-1} suggests the participation of carboxylate in the complexation. The bands at 1590 cm^{-1} and 1344 cm^{-1} assigned to the ν ($\text{COO}_{\text{asymm}}$) and ν (COO_{symm}) respectively, a shift to lower frequencies indicating the reduction of electron density in the oxygen the carboxylate group when coordinate to the metal ion. The difference between ν ($\text{COO}_{\text{asymm}}$) and ν (COO_{symm}) is greater than 140 cm^{-1} suggesting unidentate nature of acetate group. New absorption bands in the region 500-700 cm^{-1} assigned to ν (M-O) stretching vibrations.

Table.2. Selected IR frequencies (cm^{-1}) of HBT ligand and its transition metal complexes

Sl.No	Compound	ν (O-H)	ν (N-H)	ν ($\text{COO}_{\text{asymm}}$)	ν (COO_{symm})	ν (H_2O)	ν (M-O)
1	$\text{C}_{23}\text{H}_{19}\text{NO}_5$ (HBT)	-	3207	1609	1416	-	-
2	$\text{Mn}(\text{BT})_2(\text{H}_2\text{O})_2$	3891	3053	1575	1336	845	675
3	$\text{Fe}(\text{BT})(\text{H}_2\text{O})_2\text{Cl}_2$	3521	3205	1512	1380	853	649
4	$\text{Co}(\text{BT})(\text{H}_2\text{O})_4$	3621	3212	1507	1384	821	695
5	$\text{Cu}(\text{BT})(\text{CH}_3\text{COO})_4$	-	3208	1588	1406	-	655
6	$\text{Zn}(\text{BT})(\text{CH}_3\text{COO})_4$	-	3209	1562	1395	-	687

3.4. X-ray diffraction study of the compounds

Powder X- ray diffraction pattern are recorded for ligand α,α -Diphenyl- α -hydroxyacetic acid-4-hydroxyphenylalanine (HBT) and their metal chelates Mn(II), Fe(III) and Co(II). All the diffraction data are collected on Aeris research benchtop X-ray diffractometer using $\text{CuK}\alpha_1$ radiation ($\lambda = 1.5406 \text{ \AA}$) and the powder diffraction patterns for all the compounds are presented in the Figure 1-4 and respectively. Table 3-6 summarized the significant peaks of 2θ , d-spacing, and corresponding (h k l) for all three metal complexes of Mn(II), Fe(III) and Co(II).

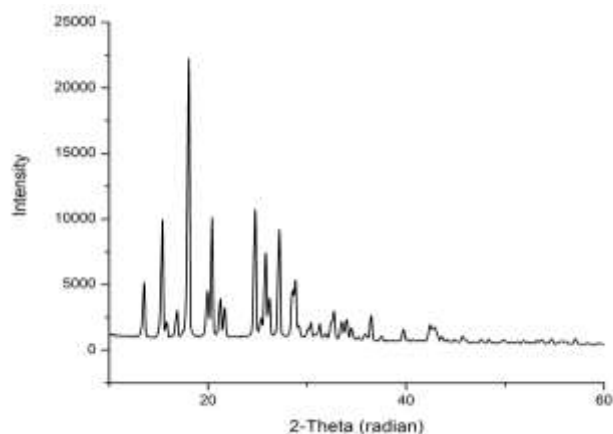


Fig 1: Crystallographic pattern of HBT

Table 3. XRD data of HBT

Crystal system: Orthorhombic

A=0.01395

B=0.003671

C=0.00279

a=6.52145

b=12.71275

c=14.58242

Cell volume: 1208.96498A³

Density: 1.013gm/cm³

No of molecules per unit cell: 2

Peak No.	2θ	Sin ² θ		d-spacing	Relative intensity	h	k	l
		Calculated	Observed					
1.	13.5464		0.01395	6.5314	23.55			
2.	15.3720	.017885	0.0179	5.7610	44.88	0	2	1
3.	16.8498	.021498	0.0215	5.2573	14.23	1	1	1
4.	18.0234	.024547	0.02455	4.9176	100	1	1	1
5.	20.3705	.031283	0.0313	2.2133	45.37	0	1	3
6.	24.7606	.046006	0.046	1.8390	48.79	1	2	2
7.	25.8038	.049899	0.0499	1.7698	35.08	0	2	1

8	27.1512	.055107	0.0551	1.6880	41.69	0	3	1
9.	28.8029	.061893	0.0619	1.5990	25.49	0	3	2
10.	32.7148	.079315	0.0793	1.4253	14.26	2	2	1
11	36.4529	.097796	0.0978	1.2963	12.58	1	4	3

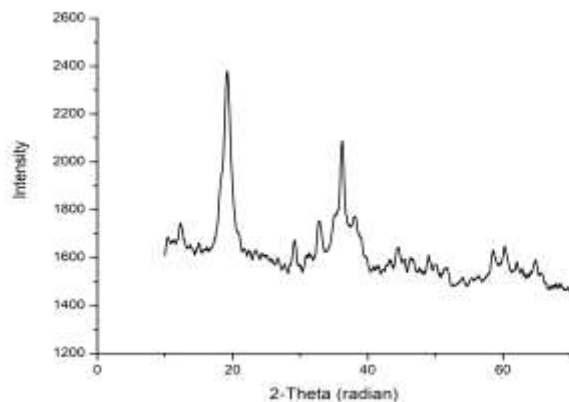


Fig 2. Crystallographic pattern of of $\text{Mn}(\text{BT})_2(\text{H}_2\text{O})_2$

Table 4. XRD data of $\text{Mn}(\text{BT})_2(\text{H}_2\text{O})_2$

Crystal system: Orthorhombic

A=0.01395

B=0.003671

C=0.00279

a=6.52145

b=12.71275

c=14.58242

Cell volume: 1208.96498Å^3

Density: 1.013gm/cm^3

No of molecules per unit cell: 2

PEAK NO	2 θ	Sin ² θ		d-spacing	Relative intensity	h	k	l
		calculated	observed					
1.	12.3728		0.0116	5.7610	73.94			
2.	19.1535	.0276	0.0276	4.6316	100	1	0	2
3.	29.1506	.0633	0.0633	3.0614	71.21	1	2	4
4.	32.6713	.079102	0.0791	2.7391	73.90	1	1	5
5.	36.1921	.096398	0.0964	2.4798	90.92	2	2	3
6.	44.49	.143351	0.14335	2.035007	70.10661	3	1	3
7.	48.92	.171453	0.17145	1.860507	68.27292	3	4	1
8.	58.49	.238698	0.2387	1.576766	69.29638	2	5	2
9.	60.35	.252650	0.25265	1.534363	69.72281	0	5	5
10.	62.09	.26555	0.26555	1.493601	67.33475	4	1	5
11.	64.92	.288088	0.2881	1.435159	67.3774	3	4	2

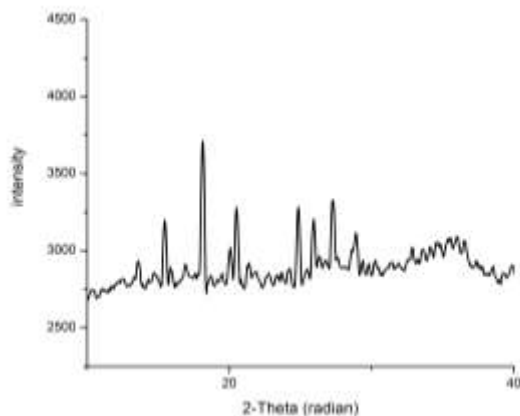


Fig 3. Crystallographic pattern of Fe(BT)(H₂O)₂Cl₂

Table 5. XRD data of Fe(BT)(H₂O)₂Cl₂

Crystal system: Orthorhombic

A=0.014 B=0.004242 C=0.002979

a=6.509800647 b=11.82623147 c=14.116226

Cell volume: 1089.289429A³Density: 1.6177gm/cm³

No of molecules per unit cell: 2

PEAK NO	2θ	Sin ² θ		d-spacing	Relative intensity	h	k	l
		calculated	observed					
1.	13.5899		0.014	6.510989	79.30295			
2.	15.4154	.017902	0.0179	5.7438	85.17	0	1	2
3.	18.1103	.024701	0.0247	4.8966	100	1	1	1
4.	20.06	.030352	0.03035	4.424182	80.67024	0	2	1
5.	20.5009	.031608	0.0316	4.3296	87.66	0	2	2
6.	24.8475	.0462	0.0462	3.5808	87.85	0	2	2
7.	25.8907	.050094	0.0501	3.4386	85.38	0	3	2
8.	27.2816	.0556	0.0556	3.2665	89.49	1	1	3
9.	28.9333	.0624	0.0624	3.0834	83.45	0	2	2
10.	32.84	.079948	0.07995	2.725584	81.3941	0	3	1

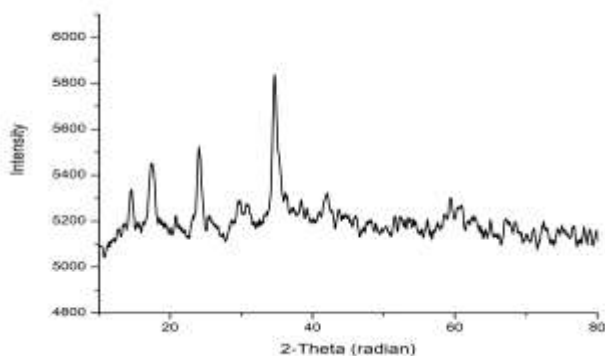


Fig 4. Crystallographic pattern of $\text{Co}(\text{BT})(\text{H}_2\text{O})_4$

Table 6. XRD data of $\text{Co}(\text{BT})(\text{H}_2\text{O})_4$

Crystal system: Orthorhombic

A=0.0157 B=0.003829 C=0.00314

a=6.14726 b=12.44769 c=13.7457

Cell volume: 1051.81119A^3

Density: 1.5346 gm/cm^3

No of molecules per unit cell: 2

PEAK NO	2 θ	Sin ² θ		d-spacing	Relative intensity	h	k	l
		calculated	observed					
1.	14.4157		0.0157	6.1423	91.04			
2.	17.3279	.022702	0.0227	5.1145	92.98	0	1	2
3.	20.7617	.032503	0.0325	4.276791	90.01208	1	1	2
4.	24.0651	.043496	0.0435	3.6960	94.72	0	2	2
5.	29.5418	.065043	0.06505	3.021773	91.06434	0	3	3
6.	34.6708	.088799	0.0888	2.5855	100	1	3	1

7.	41.9296	.128054	0.12805	2.153341	91.6681	2	3	2
8.	59.3593	.245193	0.2452	1.555746	91.44385	3	4	1
9.	62.967	.270232	0.27275	1.47501	89.85682	4	0	2
10.	65.0099	.288801	0.2888	1.433557	89.61532	4	3	1
11.	72.3556	.348436	0.34845	2.541241	89.56357	2	4	1

3.5. Antifungal study of the compounds

Among the α,α -Diphenyl- α -hydroxyacetic acid- 4-hydroxyphenylalanine complexes, Cobalt complex shows higher inhibition efficiency against the *Pencillium* sp., *Fusarium* sp. and *Pythium* sp. Copper complexes exhibits maximum efficiency for *Lasiodiplodia theobromae* and *Aspergillus* sp. All the other complexes exhibit better efficiency when compared with that of their parent ligand which clearly indicates that their inhibition efficiency has been increased upon complexation. For *Pythium* species the ligand and complexes show the following order: $\text{CoL}_1 > \text{CuL}_1 > \text{ZnL}_1 > \text{L}_1$. But in the case of *Lasiodiplodia theobromae* and *Aspergillus* sp. it exhibits an order of $\text{CuL}_1 > \text{CoL}_1 > \text{ZnL}_1 > \text{L}_1$. In the case of *Pencillium* sp. and *Fusarium* sp. the order of inhibition efficiency is $\text{CoL}_1 > \text{ZnL}_1 > \text{CuL}_1 > \text{L}_1$.

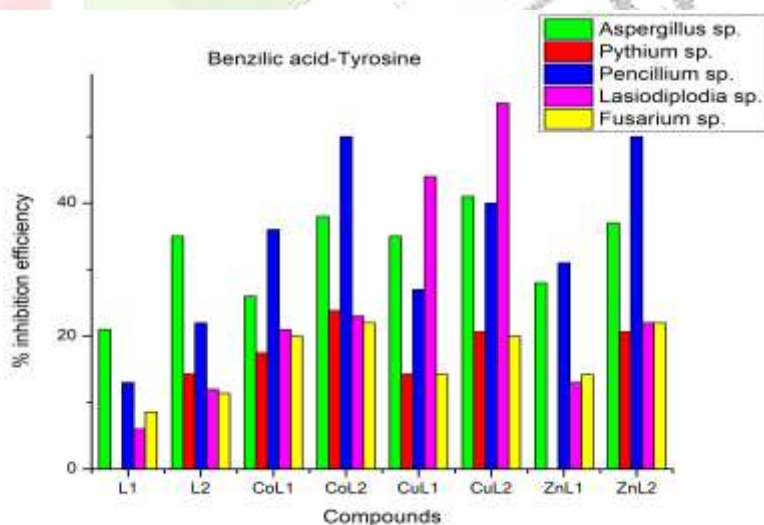


Fig.5. Fungal Inhibition efficiency of Diphenyl glycolic acid -4-hydroxyphenylalanine ligand and its metal complexes at L1 (1000ppm) and L2 (1500ppm) concentrations

Table.7. Preliminary *In vitro* antifungal activity of α,α -Diphenyl- α -hydroxyacetic acid-4-hydroxyphenylalanine ligand and its complexes against various fungal strains at 24 hour.

Fungi	Percentage of inhibition							
	L1		CoL1		CuL1		ZnL1	
Conc. (ppm)	1000	1500	1000	1500	1000	1500	1000	1500
Aspergillus niger	17	30	29	36	34	39	25	35
Phythium	-	2.22	5.55	10	4.44	6.66	-	12.32
Pencilium	3.7	11	25	29	22	25	18	25
Lasiodiplodia theobromae	26	30	34	36	39	60	30	34
Fusarium sp.	4	8	16	20	8	16	12	20

4. Conclusions

In good yields, a new series of transition metal ion complexes of the α,α -Diphenyl- α -hydroxyacetic acid-4-hydroxyphenylalanine molecule was created. Several physiochemical and structural analyses led to the conclusion that the ligands form octahedral complexes with the metal ions acting as bidentate (no donor). Furthermore, these complexes are more potent antibacterial agents than the parent ligand, as the current study clearly shows. We may conclude that the compounds synthesized and evaluated appear extremely promising because selectivity is demonstrated in the activities of some compounds over specific bacteria, which is very crucial for the future pharmaceutical applications in order to avoid the adverse effects.

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