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The Quality of Some Fungicides Containing Captan and Folpet

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Abstract: A study was conducted to investigate the degradation of Captan 50 %WP and Folpet in three fungicides (Foltex 80%, Trial F 52% and Morfy71.3%), as well as studying the formation of its impurities (Perchloromethyl mercaptan, Carbon tetrachloride and Water) before and after storage at 54±2°C for 21 days. Captan and Folpet is a fungicide used for the control of fungal diseases in crops. The obtained results showed that Captan was more stable after storage. The Perchloromethyl mercaptan in Captan formulation was more than the maximum permissible concentration of impurity recommended by FAO specifications before storing but decreasing during storage, which become less than the maximum permissible FAO specifications. While, Carbon tetrachloride in three of the commercial formulations of Folpet (Foltex, Trial F and Morfy) before storage was more than the FAO maximum level, which becomes less than the maximum permissible FAO specifications for fungicide Trial F after storage. Nevertheless, those levels are still higher them matching the FAO maximum level for Foltex and Morfy, there is impurities water which less than the maximum permissible FAO specifications before and after storage for all Folpet formulations. On the other hand, GC – MS was used to compare the fragmentation of two the fungicide formulation (Captan and Folpet) and results showed that of the breakdown of Tetrahydrophthalimide THPI (main product) in Captan formulation. While of phthalimide PI (main product) in Folpet formulation.

Key words: Captan · Folpet · Foltex · Trial F and Morfy and toxic impurities

INTRODUCTION

Captan is a nonspecific sulfenimidc fungicide. It is applied to control diseases of vegetable crops, fruits and ornamentals [1]. Captan reaction with thiol groups has been pointed out as the main mode of action on phytopathogenic fungi, been responsible for the reduction of enzymatic activities, respiration, physiological changes and fungal death [2]. In the presence of exposed thiol groups, captan oxidize thiols and is hydrolyzed to its reactive thiophosgene ($SCCl_3$) moiety and the 1, 2, 3, 6-tetrahydrophthalimide ring [3]. *In vitro* genotoxicity studies indicated that phthalimide fungicides were associated to point mutations and gene conversion [4], been classified as a potential human carcinogen. However, based on in vivo and molecular analysis in mammals they were re-classified as nongenotoxic [5].

Folpet belongs to the sulfenimide group of pesticides also containing captan and captafol [6]. It was first introduced in 1952, folpet has been widely employed on grapevines and other fruit trees [7]. In France, it still plays an important role in preventing the fungi-caused diseases in grapes, with the spraying frequency of 10 to 15 times from May to September [8].

Significant numbers of the fungicide released to the environment are chiral. Two enantiomers of the each of the chiral compounds were separated from folpet, very commonly present in fungicide formulation containing metalaxyl or benalaxyl, the activity and toxicity of the different enantiomers are different in this regard chiral analysis is influence and certain form for studying the behavior of environmental pollutants during biological and environmental processes [9].

Perchloromethyl mercaptan impurities in captan is mainly used as intermediate for the synthesis of fungicides (Captan, folpet) it is an oily pale-yellow liquid, which is insoluble in water with foul-smelling, unbearable, acrid odor when it is heated or in fire it will emit toxic and corrosive gases, it is also very toxic by inhalation or skin adsorption [10].

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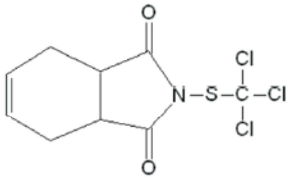
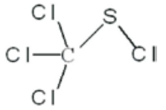
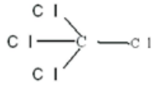
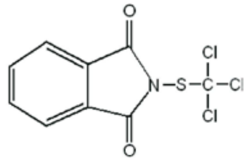
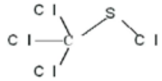
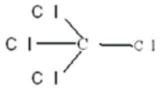
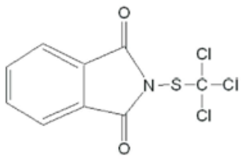
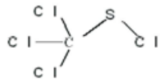
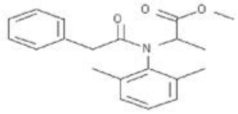
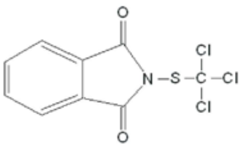
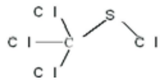
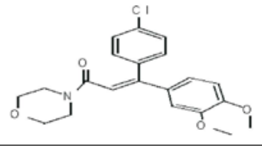
Heterogeneous OH oxidation of folpet and dimethomorph results in the regeneration of the latter lead to formation methanone as well as other product N-formyl morphline, which is transferred to the gaseous phase, this dimethomorph may be considered a source of secondary pollution in the atmosphere [11].

In, the present study aimed to evaluate the effect of storage on the degradation of Captan, Folpet and their content of impurities of Perchloromethyl mercaptan, carbon tetrachloride and water. In addition, captan and Folpet formulation have been determined by GC/MS.

MATERIALS AND METHODS

Fungicides Used: Table (1) the tested fungicides and their impurities:

Trade name	Common name	Structure	Impurities	Structure
Captan 50% (WP)	Captan		*Perchloromethyl mercaptan. FAO max= 1% of captan content **carbon tetrachloride	 
Foltex 80%(WG)	Folpet 80%		*Perchloromethyl mercaptan. ***Water *carbon tetrachloride FAO max= 4 g/kg of folpet content	 
Trial F 52% (WG)	A- Folpet 44 %		*Perchloromethyl mercaptan. *carbon tetrachloride ***Water	 
	B-Benalaxyl 8 %		UND	UND
Morfy 71.3% (WP)	A- Folpet 60 %		*Perchloromethyl mercaptan. *carbon tetrachloride ***Water	 
	B-Dimethomorph			

WP = wettable powder WG= water granules

Storage Stability Test: The samples of captan, folpet, benalaxyl and dimethomorph were stored at 54 ± 2°C for 21days according to FAO [12, 13, 14, 15]. The active ingredient and the toxic impurities content of the samples were determined at 0, 3, 7, 14 and 21 days of the storage.

Preparation of the Sample

Standard Preparation: Weight 10 mg of the analytical standard for all tested pesticides and their impurities (Captan, Folpet, Benalaxyl, Dimethomorph, Perchloromethyl mercaptan and carbon tetrachloride) weighted inside a different six 25 ml volumetric flask then dissolve it and completed to the final volume with methanol.

Sample Preparation for Tested Pesticides: Enough sample was weighed accurately equivalent to 10 mg of standard in a different 25 ml volumetric flask for each sample and slowly mixed with methanol and the volume was completed with methanol.

Sample Preparation for Impurities: One ml tested formulation samples (Captan 50% (WP), Foltex 80% (WG), Trial F 52% (WG) and Morfy 71.3% (WP)) was weighed, which contain 0.5 g, 0.8 g, 0.52 g and 0.71 gm of Captan, Foltex, Trial F and Morfy, respectively in a four different 25ml volumetric flasks, dissolved with methanol and completed to the final volume with methanol.

Gas Chromatography Determination for Captan, Foltex and Trial F (Benalaxyl, Folpet): A Hewlett – Packard G. C. Model 6890 instrument, equipped with a flam ionization detector (FID), capillary column 15 m × 0.53 mm. nitrogen was used as a carrier gas at a flow rate of 7 ml/min. oven temperature 200°C. Under these conditions, the retention time of Captan, Foltex, Benalaxyl and Folpet were 1.8, 1.7, 3.5 and 1.7 min respectively. The quantitative determination by comparison with the standard of known purity under the identical GLC condition.

HPLC Instrument Determination of Dimethomorph, Perchloromethylmercaptan and Carbon Tetrachloride: The active ingredient percentage for Dimethomorph, Perchloromethyl mercaptan and Carbon tetrachloride were determined before and after storage, according to the method of Tan Wei [16] with Some modification an Agilent serious 1100 quarterly pump with the ultraviolet (U.V) detector and a C_{18} stainless steel column 2.6 X_{mm} 25 cm was used. Acetonitrile – Methanol (70:30) v/v was used as a mobile phase for dimethomorph and Perchloromethyl mercaptan; but was use Acetonitrile – Methanol (80: 20) v/v for carbon tetrachloride, at the rate of 0.8 ml/min, 40°C column temperature and wavelength 197, 210 and 235nm. At this condition, the retention time (Rt) of the dimethomorph, Perchloromethyl mercaptan and carbon tetrachloride were 1.613, 1.79 and 2.14, respectively.

Gas - Chromatography-mass Spectrometry Analysis of Captan and Folpet: The GC - MS analysis was performed with an Agilent of 6890 gas chromatography equipped with an Agilent mass spectrometric detector, with the direct capillary interface and fused silica capillary column HP-5MS (30 m x 320 mm × 0.25 mm film thickness). Helium was used as carrier gas at approximately 1.0 ml/min pulsed splitless modes. The solvent delay was 3 min and the injection volume was 1µL. The mass spectrometric detector was operated in electron impact ionization mode with the ionizing energy of was 70 e.v scanning from m/z 50 to 500. The ion source temperature was 230°C and quadruples temperature 50°C. The electron multiplier voltage (EM voltage) was maintained 1050 v above autotune. The instrument was manually tune using perfluorotributylamine (PFTBA). The GLC temperature program was held at 80°C for 3 min, then elevated to 260°C at a rate of 80°C/ min, the detector and injector temperature was set at 280 and 250°C, respectively [17].

Determination of Water Impurity in Foltex 80%, Trial F 52% and Morfy 71.3%: Water content as relevant impurities for folpet in foltex 80%, Trial F 52% and Morfy 71.3% was determined by Dan strak method as mentioned in CIPACF [19].

RESULTS AND DISCUSSION

Effect of Storage on the Stability of Captan and its Contents: Data presented in Table (2) showed that the stability of captan active ingredient in its formulation was relatively influencing during storage at 54± 2°C, where the percentage loss of captan after 21days of storage was 0.86 %.

Furthermore, the results in a Table (2) showed that the amount of Perchloromethyl mercaptan before storage was 1.9 % of captan content. This level is higher matching the maximum level (1% of captan content) which defined by FAO [12], the data also showed decreasing the amount of impurities during storage periods, which become 0.6% of captan content after 21 days of storage at 54 ± 2°C, such the amount is lesser than the maximum level.

These results in agreement with Ravichandran *et al.* [19] decreasing yield of Perchlormethylmercaptan $SCCl_3$ at elevated temperatures suggests that further reaction relating to $SCCl_3$ can take place. The oxidation of $SCCl_3$ by oxygen was reported to form SO and CCl_3 radical has been extensively studied because of its importance in atmospheric pollution [20].

The data in Table (2) showed that the level of carbon tetrachloride as g/kg of captan content was 13.8 g/kg before storage that decreased during the storage period to reach 6.0 g/kg of captan content after 21 days of storage at 54 ± 2°C; this level of carbon tetrachloride was not defined by FAO for captan.

Table 2: Effect of storage at 54 ± 2°C for 21 days on the stability of Captan and its contents:

Storage periods (days)	Captan 50%	Loss %	Perchloromethyl mercaptan	*Perchlormethyl mercaptan as % captan content	CCl_4	** CCl_4 as g/kg Captan content
0	49.89	-	0.94	1.9	0.69	13.8
3	49.81	0.16	0.81	1.6	0.67	13.4
7	49.66	0.46	0.40	0.8	0.55	11.1
14	49.51	0.76	0.37	0.7	0.40	8.0
21	49.46	0.86	0.34	0.6	0.30	6.0

Zero = one hour before storage.

* Perchlormethylmercaptan as %= % perchlormethyl mercaptan ÷ % Captan × 100

** CCl_4 as g/kg =CCl_4÷ Captan × 1000

Table 3: Effect of storage at 54 ± 2°C for 21 days on the stability of Foltex and its contents:

Storage periods (days)	Folpet 80%	Loss%	Perchloromethyl mercaptan	*Perchlormethyl mercaptan as % foltex content	CCl_4	** CCl_4 as g/kg foltex content
0	79.83	-	0.72	0.9	1.03	12.9
3	79.56	0.43	0.63	0.8	1.01	12.6
7	79.42	0.51	0.60	0.7	0.98	12.3
14	79.11	0.90	0.38	0.5	0.75	9.4
21	77.34	3.11	0.35	0.4	0.66	8.5

Zero: one hour before storage

* Perchlormethylmercaptan as %=% Perchlormethylmercaptan ÷ Foltex × 100

** CCl_4 as g/kg =CCl_4÷ Folpet × 1000

Effect of Storage on the Stability of Foltex and its Contents: Data illustrated in Table (3) show that the initial of folpet active ingredient in its formulation was 79.83% before storage and reached to 77.34% after storage at 54 ± 2°C for 21 days with percentage loss is 3.11%.

Also, the results in Table (3) showed that the amount of Perchloromethyl mercaptan before storage was 0.9 % of folpet content., the data also showed decreasing the amount of impurities during storage periods, which become 0.4% of folpet content after 21 days of storage at 54 ± 2°C, this level of Perchloromethyl mercaptan was not defined by FAO for folpet.

Data also in the Table (3) showed that the level of carbon tetrachloride as g/kg of folpet content before storage was 12.9 g/kg, this level higher than the maximum level (4 g/kg of folpet content) defined by FAO [13]. The data showed decreasing the amount of impurities during the storage period that becomes 8.5g/kg of folpet content after 21 days of storage at 54 ± 2°C, nevertheless, those levels are still higher them matching the FAO maximum level.

Effect of Storage on the Stability of Trial F and its Contents: In Table (4) it was shown that the stability of trial f (a mixture of Folpet 44 % and Benalaxyl 8%) found that the stability of folpet active ingredient was relatively influencing during storage at 54±2°C where the percentage loss of folpet after 21 days of storage was 1.05%, data also show that the stability of benalaxyl where the percentage loss of benalaxyl after 21 days of storage was 1.25%.

In addition, the results in a Table (4) showed that the amount of Perchloromethyl mercaptan before storage was 2.3% of folpet content. The data decreasing the amount of impurities during the storage periods, which become 0.5% of folpet content after 21days of storage, this level of Perchloromethyl mercaptan was not defined by FAO for folpet.

NIOSH [21] Found that Hazardous decomposition products: Toxic gases and vapors (such as carbon tetrachloride, hydrogen chloride, sulfur monochloride, carbon monoxide and sulfur dioxide) may be released in a fire involving Perchloromethyl mercaptan.

Data also in the Table (4) showed that the level of carbon tetrachloride as g/kg of folpet content before storage was 6.3 g/kg of folpet content, this level higher than the maximum level (4 g/kg of folpet content) defined by FAO [13]. The data showed decreasing the amount of impurities during the storage period, which becomes 3.7 g/kg of folpet content after 21 days of storage at 54 ± 2°C, such the amount is less than the maximum level.

Effect of Storage on the Stability of Morfy and its Contents: Data present in Table (5) showed that the stability of morfy (a mixture of Folpet 60% and dimethomorph 11.3%) found the stability of folpet active

Table 4: Effect of storage at 54±2°C for 21 days on the stability of Trial F and its contents:

Storage period (days)	Flopet 44%	Loss %	Perchloromethyl mercaptan	*Perchlormethyl mercaptan as % Folpet content	CCl_4	**CCl_4 as g/kg Folpet content	Benalaxyl 8%	Loss%
0	43.91	-	0.99	2.3	0.28	6.3	7.98	-
3	43.76	0.34	0.96	2.2	0.26	5.9	7.95	0.38
7	43.61	0.68	0.75	1.7	0.23	5.3	7.92	0.75
14	43.55	0.82	0.55	1.3	0.18	4.1	7.89	1.13
21	43.45	1.05	0.20	0.5	0.16	3.7	7.88	1.25

Zero: one hour before storage

* Perchlormethylmercaptan as % = % Perchlormethylmercaptan ÷ Folpet × 100

** CCl_4 as g/kg =CCl_4÷ Folpet × 1000

Table 5: Effect of storage at 54±2°C for 21 days on the stability of Morfy and its contents:

Storage period (days)	Folpet 60%	Loss %	Perchloromethyl mercaptan	*Perchlormethyl mercaptan as % folpet content	CCl_4	**CCl_4 as g/kg folpet content	Dimethomorph 11.3%	Loss %
0	59.58	-	1.24	2.0	3.6	60	11.25	-
3	58.88	1.1	1.04	1.8	3.3	56	11.17	0.71
7	57.29	3.84	0.97	1.7	2.9	50	10.81	3.91
14	56.74	4.77	0.62	1.1	2.3	40	9.89	12.1
21	56.29	5.52	0.39	0.7	1.6	28	9.60	14.7

Zero: one hour before storage

* Perchlormethylmercaptan as %=% Perchlormethylmercaptan ÷ Folpet × 100

** CCl_4 as g/kg =CCl_4÷ Folpet × 1000

ingredient was relatively influencing during storage at 54 ± 2°C where the percentage loss of folpet after 21 days of storage was 5.52%, data also show that the stability of dimethomorph where the percentage loss of dimethomorph after 21 days of storage was 14.7%.

In addition, the data in the Table (5) stated that the amount of Perchloromethyl mercaptan before storage was 2.0% of folpet content. The data decreasing the amount of impurities during the storage periods, which become 0.7 % of folpet content after 21days of storage, this level of Perchloromethyl mercaptan was not defined by FAO for folpet.

Also, the results in a Table (5) showed that the level of carbon tetrachloride as g/kg of folpet content before storage was 60 g/kg of folpet content, this level higher than the maximum level (4 g/kg of folpet content) defined by FAO [13]. The data showed decreasing the amount of impurities during the storage period that becomes 28 g/kg of folpet content after 21 days of storage at 54 ± 2°C, nevertheless, those levels are still higher them matching the FAO maximum level.

Increase the CCl_4 before storage due to industry this results in agreement with IPPCS [22] who showed that relevant impurities (Perchloromethyl mercaptan and carbon tetrachloride) are a by-product of the manufacturing process for folpet and captan as such cannot be formed by storage of the formulation. High levels of $CCl4$ is lost from surface water by volatilization, other levels in anaerobic groundwater may remain elevated for months or even years.

Estimation of Water as Relevant Impurities of Folpet in Foltex 80 %, Trial F 52% and Morfy 71.3 %: It should be determined water content with dean and stark method CIPAC F [18]. where water might a diversely affect storage stability or, in the case water granules (WG) and wettable powder (WP) were decreased, where the subsequent formulation of the active ingredient-containing to much water could lead to an unacceptable product. Furthermore, during extended storage degradation product may be formed, which pose toxicological hazards to consumers of treated food for safety and efficacy assessment in agreement with FAO [23] and Ambrus *et al.* [24].

The data presented in table (6) indicate that the result of water content in foltex (WG), trial F (WG) and morfy (WP) before storage were 0.66, 0.2 and 0.33 g/kg, respectively and decreased to 0.33 and 0.06 g/ kg for foltex and morfy after storage for 21days at 54±2°C. While undetectable for trial F these may be due to lower moisture content. Data indicated that tested foltex (WG), trial F (WG) and morfy (WP) passed successfully through impurities value and complies with FAO [13] before and after storage and maximum permissible limits 50 g/ kg for folpet has been justified and not exceed their maximum permissible limits, while Captan is not relevant.

Table 6: Effect of storage on water impurities of Folpet in Foltex, Trial F (WG) and Morfy (WP):

	Foltex (WG)		Trial F (WG)		Morfy (WP)		
Impurities	Before Storage	After Storage	Before Storage	After Storage	Before Storage	After Storage	Captan (WP)
Water cotent	0.66	0.33	0.2	UND	0.33	0.06	Not relevant

Identification of Captan and Folpet by Chemical Ionization GC/MS Spectroscopy:

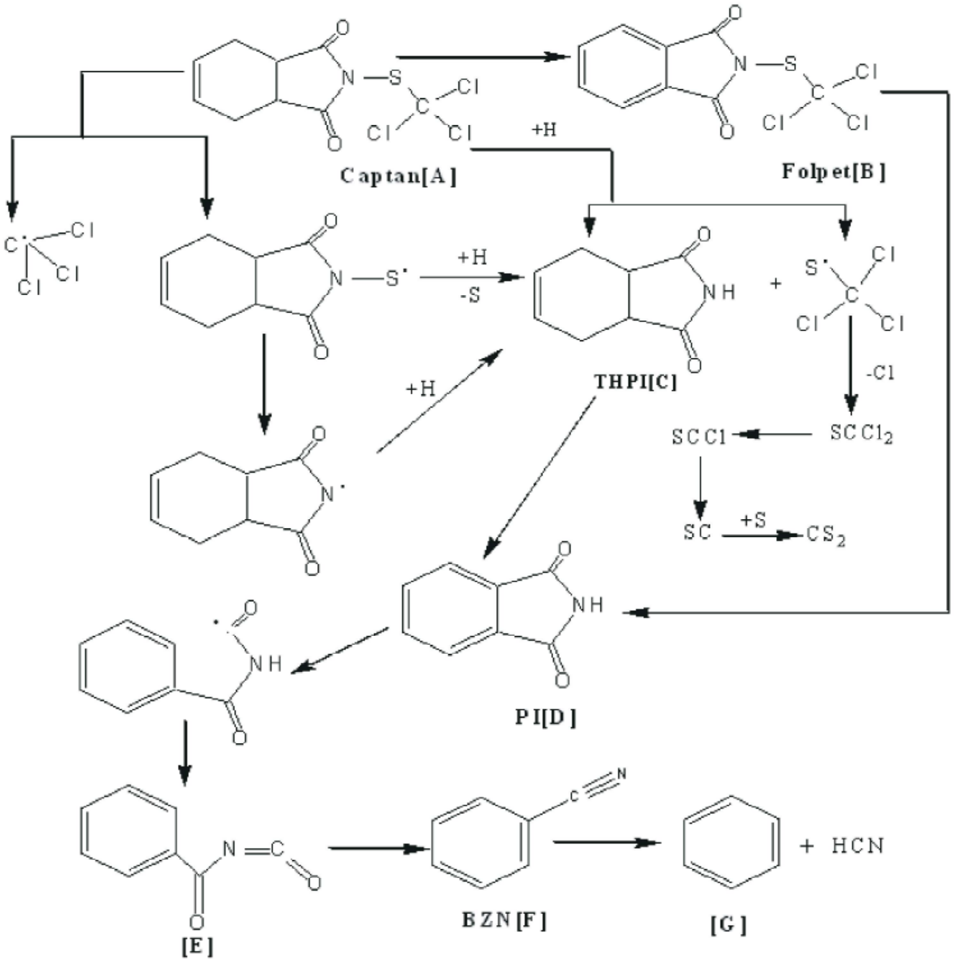


Fig. 1: Fragmentation of Captan and Folpet

Fragmentation hypothesized to rationalize through:

Figure (1): described possible reaction pathways leading to the degradation of Captan and Folpet, such as:

- Oxidation of captan m/z 300.59 leads to a product of Folpet m/z (296.56). The degradation of captan [A] proceeds by cleavage of the N-S bond to form tetrahydrophthalimide THPI[C] m/z 151.16 and a derivative of the -SCCl3 side chain.
- The cleavage of THPI [C] to form phthalimide PI [D] m/z 147.13.
- The degradation of folpet [B] proceeds by The cleavage of the N-S bonds to form phthalimide (PI) [D] lead to form Benzoylisocyanate [E] m/z 147.13 which converts into Benzene (BZN) m/z 78.11 [F] proceeds by cleavage of the C-N lead to formation benzene [G] m/z 78.11.

The only difference in the two compounds (captan [A] and folpet [B]) being that the ring portion of folpet is aromatic; so it has been assumed that all degradation data for captan relative to the trichloromethylthio portion of the molecule will also be applicable to folpet.

Table 7: Identification of Captan and Folpet by chemical ionization GC/MS spectroscopy:

	Captan			Folpet		
Storage periods	Captan degradation	Retention time(Min)	Formula	Folpet degradation	Rt (Min)	Formula
Initial	Captan m/z(300.59)	26.6	$C_9H_8Cl_3NO_2S$	Folpet m/z(296.56)	24.5	$C_9H4Cl_3NO_2S$
	Tetrahydrophthalimide (THPI) m/z(151.16)	25.2	$C_8H_9NO_2$	Phthalimide(PI) m/z(147.13)	22.4	$C_8H_5NO_2$
After 21 days of storage at 54°C	Captan m/z(300.59)	26.9	$C_9H_8Cl_3NO_2S$	Folpet m/z(296.56)	24.2	$C_9H_4Cl_3NO_2S$
	Folpet m/z(296.56)	24.2	$C9H4Cl_3NO_2S$	(PI) m/z(147.13)	22	$C_8H_5NO_2$
	(THPI) m/z(151.16)	25.6	$C_8H_9NO_2$	Benzoyl isocyanate m/z(147.13)	16.5	$C_8H_5NO_2$
	(PI) m/z(147.13)	16.4	$C_8H_5NO_2$	Benzonitrile(BZN) m/z(103.12)	15.7	C_7H_5N
	Benzoylisocyanate m/z(147.13)	16.2	$C_8H_5NO_2$	Benzene m/z(78.11)	15.4	C_6H_6
	Benzonitrile(BZN) m/z(103.12)	15.4	C_7H_5N			
	Benzene m/z(78.11)	14.7	C_6H_6			

Initial: one hour before storage

Both folpet and captan incorporate the trichloromethylthio ($SCCl_3$) group. Folpet is the aromatic version of captan, with the $SCCl_3$ group bonded to a phthalimide (PI) moiety rather than to the tetrahydrophthalimide (THPI) group in captan. With its stronger C-H bonds and hence less abstractable hydrogen on the aromatic ring, folpet would be expected to yield similar products because of the reactions involving the $SCCl_3$ group and to exhibit different products arising from reactions of chemically dissimilar THPI and PI moieties. These results are in agreement with Venna *et al*. [25] who showed that organism degraded captan by a pathway involving it is initial hydrolysis to yield cis 1, 2, 3, 6- tetrahydrophtalimid (THPI), a compound without fungicidal activity. The formation of this compound was confirmed by NMR and Mass spectral analysis.

In the Table (7) it was shown that retention time (Rt) of captan m/z (300.59) was 26.6 min before storage and shift to 26.9 min after storage 21 days at 54±2°C.

Also, in the Table (7) shown that Rt of breakdown product (Main product) Tetrahydrophthalimide (THPI) in Captan was 25.2 min before storage and shift to 25.6 min after storage 21 days at 54±2°C.

Data, also in the Table (7) indicated that Rt of the breakdown of folpet m/z (296.56) was 24.5 min before storage and shift to 24.2 min after storage 21 days at 54±2°C. Also, in the Table (7) shown that Rt of breakdown product (Main product) Phthalimide (PI) in folpet was 22.4 min before storage and shift to 22 min after storage 21 days at 54±2°C. There is no difference in the rate of degradation for all folpet formulations under investigation.

Chen *et al*. [26] have studied both folpet and captan incorporates the trichloromethylthio ($SCCl_3$) group. Folpet is the aromatic version of captan, with the $SCCl_3$ group bonded to a phthalimide (PI) moiety rather than to the tetrahydrophthalimide (THPI) group in captan. We have previously determined the toxic air pollutants from the oxidation of captan and discovered that the abstraction of hydrogen atoms from the cyclohexene ring may facilitate the decomposition process.

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