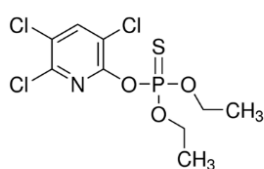
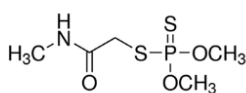


Supporting Information 1

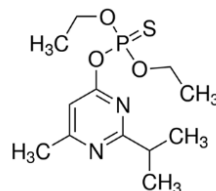
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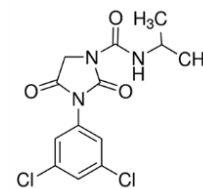
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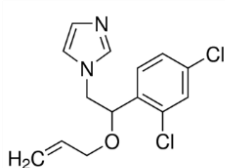
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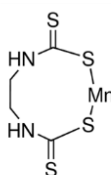
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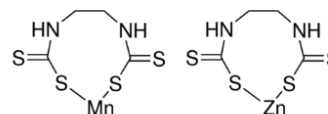
Iprodione



Imazalil



Maneb



Mancozeb

Cell cultures:

Primary normal BM-MSCs were isolated from healthy donors (without any hematological disorder) undergoing orthopedic surgery (University Hospital, Tours, France) after informed consent and following a procedure approved by the local ethical committee. BM-MSCs were amplified as previously described (Delorme and Chabord, 2007). MSCs (used between passages 4 and 7) were cultured at 2,000 cells per cm² in α -MEM modified with ribonucleosides and deoxyribonucleosides and supplemented with FCS (10%) and 2 mM L-glutamine, 100 U/ml penicillin, 100 μ g/ml streptomycin, and 0.2 ng/ml of FGF2.

Peripheral blood mononuclear cells were obtained from two human buffy coat (Etablissement Français du Sang, Rennes, France) by differential centrifugation on UNI-SEP maxi U10 (Novamed, Jerusalem, Israel). The experiments were performed in compliance with the French legislation on blood donation and blood products' use and safety. Monocytes from healthy donors were enriched using a human CD14 separation kit (Microbeads; Miltenyi Biotec, Bergisch Gladbach, Germany), plated at a density of 0.5×10^6 cells per well in 24-well plates and cultured at 37 C with 5% humidified CO₂ in RPMI 1640 medium supplemented with 100 IU/ml penicillin–100 mg/ml streptomycin, 2 mM L-glutamine and 10% FCS BioWhittaker®. Macrophages were obtained after differentiation from monocytes by incubation with 50 ng/mL

rhGM-CSF in RPMI 1640 medium during 7 days, as previously described (Vène et al., 2016). All cells were cultured at 37°C in a 5% CO₂ atmosphere.

HepG2 and Huh7 human hepatoma cell line were cultured in Dulbecco's Modified Eagle Medium (DMEM) supplemented with 10% FBS, 1% glutamine (200mM), 100U/ml penicillin, 100µg/ml streptomycin.

Rat liver epithelial cells (RLEC) were obtained as previously described from rat livers (Corlu et al., 1991) and maintained in William's E medium supplemented with 10% Fetal calf serum, 100 units/mL penicillin, 100µg/mL streptomycin, 2mM L-glutamine.

List of forward and reverse primers used for RT-qPCR:

Supporting Information 2

	Primer sequence	
	Forward	Reverse
BAX	5'-GGA-GCT-GCA-GAG-GAT-GAT-TG-3'	5'-AGT-TGA-AGT-TGC-CGT-CAG-AA-3'
DDIT3	5'-GTC-TAA-GGC-ACT-GAG-CGT-ATC-3'	5'-CAC-TTC-CTT-CTT-GAA-CAC-TCT-CT-3'
GPX3	5'-CAA-CCC-TTT-CTC-TCC-AGT-TCT-C-3'	5'-CCC-AAG-GTT-GAG-GTA-TCA-GTT-AG-3'
SOD1	5'-GAA-AAC-ACG-GTG-GGC-CAA-AG-3'	5'-GCA-GTC-ACA-TTG-CCC-AAG-TC-3'
SOD2	5'-TTG-CTG-GAA-GCC-ATC-AAA-CG-3'	5'-GAA-ACC-AAG-CCA-ACC-CCA-AC-3'
TBP	5'-GAG-CTG-TGA-TGT-GAA-GTT-TCC-3'	5'-TCT-GGG-TTT-GAT-CAT-TCT-GTA-3'

Genotoxicity assay using γ -H2AX staining:

The γ -H2AX staining was used to monitor genotoxicity. After 24 hours of treatment, cells were washed with PBS and then fixed with 4% PAF for 15 minutes at RT. Cells were permeabilized with PBS containing 0.1% Triton X-100 for 5 minutes at RT, rinsed twice and then blocked with FBS 10% in 0.1% PBS-Tween 20 for 1h at RT. Cells were washed twice with PBS 0.1% Tween 20 and then incubated overnight at 4°C with Anti-gamma H2A.X (phospho S139) antibody [EP854(2)Y] (Alexa Fluor 488) ab195188 (abcam) at 1/50 dilution or with non-immune control antibodies labeled with Dylight 488 at 1/250 dilution. Antibodies were diluted in PBS 0.1% Tween 1% BSA. After two washes, nuclear DNA staining was performed using Hoechst 33342 at 10µg/mL in PBS 0.1% Tween 20. Then, cells were washed with PBS and γ -H2AX positive foci were observed by fluorescence microscopy using Zeiss Inverted Microscope and photographs were analyzed with the AxioVision Software.

Detection of cells with sub-G1 DNA content by flow cytometry:

Apoptotic cells with hypoploid DNA content were detected by flow cytometry using propidium iodide. Briefly, after 24 hours of treatment, cells were collected and DNA was labeled using the BD Cycletest Plus DNA Kit (BD Bioscience ref: 340242). The fluorescence intensity of 10,000 cells was analyzed with a Becton Dickinson le LSRFortessa™ X-20 (cytometry core facility of the Biology and Health Federative research structure Biosit, Rennes, France).

Buffers and substrates used for measurement of mitochondrial OXPHOS complex enzyme activities:

Complex	I	II	III	IV	V	CS
Potassium dihydrogen phosphate	80mM pH 7.4	50mM pH 7.5	10mM pH 7.8	-	20mM pH 8.1	-
Adjuvants	BSA 1mg/mL	BSA 1mg/mL EDTA 0.1mM	BSA 1mg/mL EDTA 2mM Lauryl maltoside 0.6mM	BSA 1mg/mL Lauryl maltoside 2.5mM	MgCl ₂ 1mM KCl 2mM Pyruvate kinase 1U/mL LDH 1.7U/mL PEP 0.4mM FCCP 0.15mM	Oxaloacetate 0.5mM Triton X100 0.1%
Inhibitors	KCN 1mM Azide 2mM Rotenone 10 µM	KCN 2mM Rotenone 10µM Antimycin 2µM	KCN 0.24mM ±Antimycin 4µg/mL		Antimycin 0.1µg/mL ±oligomycin 0.01µg/mL	
Substrats	Decylubiquinone 0.1m DCPIP 75µM NADH 30µM	Succinate 20mM DCPIP 80µM Decylubiquinone 60µM	Cytochrome C 40µM Decylubiquinol 0.1mM	reduced Cytochrome C 50µM	NADH 0.15mM ATP 0.2mM	DTNB 0.15mM ACoA 0.3mM

BSA : bovine serum albumin ; DCPIP : 2,6-dichlorophenolindophenol ; KCl : potassium chloride ; KCN : potassium cyanide ; LDH : lactate dehydrogenase ; MgCl₂ : magnesium chloride ; PEP : phosphoenolpyruvate

References in Supporting information 1:

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Delorme B, Charbord P. Culture and characterization of human bone marrow mesenchymal stem cells. *Methods Mol Med.* 2007; 140:67-81. doi: 10.1007/978-1-59745-443-8_4.

Vene E, Barouti G, Jarnouen K, Gicquel T, Rauch C, Ribault C, Guillaume SM, Cammas-Marion S, Loyer P. Opsonisation of nanoparticles prepared from poly(β-hydroxybutyrate) and poly(trimethylene carbonate)-b-poly(malic acid) amphiphilic diblock copolymers: Impact on the in vitro cell uptake by primary human macrophages and HepaRG hepatoma cells. *Int J Pharm.* 2016 Nov 20;513(1-2):438-452. doi: 10.1016/j.ijpharm.2016.09.048.

Supporting Information 2

Metabolism of mancozeb in hepatocyte-like HepaRG cells.

Based on bibliographic data (references below), 12 metabolites that can be formed during the catabolism of mancozeb have been inventoried. Among these 12 compounds, eight have analytical standards that were purchased and analyzed in this study (Table 1). Ethylene thiourea (ETU) (99,6% purity), mancozeb (70.1%), EDA (100%), N-acetyl-EDA (100%), allantoin (100%), glycine (100%) and creatinine (99.1%) were purchased from Dr. Ehrenstorfer GmbH, EBIS (100%) from Toronto Research Chemicals. Formic acid, methanol and water were HPLC/MS-grade, and were purchased from J.T. Baker (Paris, France).

The analysis was performed by direct injection in UPLC/MSMS with a Xevo-TQD® triple quadrupole (Waters) in MRM (Multiple Reaction Monitoring) mode. The mode of ionization retained is positive electrospray.

Chromatographic separation was done with a Waters Acquity UPLC HSS-T3 C18 column (2.1mm x 150 mm, particle size 1.8 µm, Waters®) maintained at 30 °C. The mobile phase was a gradient of water/0.01% formic acid (v/v) (A) and methanol /0.05% formic acid v/V (B) with a flow rate of 0.2 mL/min. The elution gradient started with 95% eluent A, maintaining isocratic conditions for 2 minutes. Then eluent B increased to 100% in 7 minutes and was maintained for 2.50 minutes. Finally, initial conditions were reached again in 0.10 minutes with a re-equilibrium time of 3.4 minutes to restore the column. The injection volume was 5 µL.

For the mass detector, the parameters were as following: Source temperature 150 °C, desolvation temperature 650 °C, cone gas flow 50 L/h, desolvation gas flow 800 L/h, spray voltage 1kV.-

For each compound, distinctive ions and transitions were selected for identification (MRM2) and quantification (MRM1), as well as for confirmation purposes.

Dimethyl-sulfoxide (DMSO) was the solvent for ETU, mancozeb, hypoxanthine to prepare stock solution at 1mM and a mixture of water and 0.1% NAH4OH for xanthine and uric acid.

The injection of analytical standards (at a concentration of 10 µM in water) allowed to define the analytical features of the 8 metabolites and active substance (table 1) and to estimate their limits of quantification. 9 concentrations (0.01 to 10 µM in a mixture water/ William's E Medium 50/50 v/v)) were injected to determine the calibration function. Data was best fitted with a quadratic calibration except for ETU (cubic function). A control (5 µM) was injected every 15 samples.

This method was applied to samples, in culture media containing or not mancozeb and incubated or not with HepaRG cells with direct injection (5µL).

Mancozeb / metabolites	CAS n°	Rt (min)	Cv (V)	Precursor ion	MRM1	MRM2	LoQ (μ M)
Mancozeb	8018-01-7	8.7	40	213	213>86 (25)	213>169 (17)	0.01
Ethylenediamine (EDA)	107-15-3	1.5	20	61	61>44 (30)	-	11
Glycine	56-40-6	1.6	22	76	76>30 (8)	76>48 (8)	n.d.
N-acetyl-EDA (N-(2-aminoethyl)acetamide)	1001-53-2	1.6	20	103	103>44	103>43	11
Allantoin	95-59-6	1.8	25	157	157>97 (12)	157>114 (10)	3
Creatine	57-00-1	1.8	30	132	132>44 (16)	132>90 (12)	0.1
EU – ethylene urea	120-93-4	2.6	45	87	87>44 (12)	87>42 (15)	0.2
ETU – ethylene thiourea	96-45-7	3.0	30	103	103>44 (14)	103>60 (21)	0.1
EBIS (ethylene bisisothiocyanate sulfide)	33813-20-6	8.9	40	177	177>43 (22)	177>101 (20)	0.1

Table 1 : Detection parameters of mancozeb and its metabolites (Rt: retention time; Cv: cone voltage; MRM1 quantification (uma) (collision energy - eV); MRM2 confirmation (uma) (collision energy - eV); LoQ:Limit of Quantification; n.d.: not determined)

Analyses showed that EU, EDA, N-Acetyl-EDA, allantoin and EBIS were absent of all samples analysed. Glycine was found in all media at nearly identical amounts because this amino acid is a component of the Williams E medium used for the culture of HepaRG cells (concentration in the medium 0.66 mM). Creatine is also found in culture media incubated with cells regardless of the incubation with mancozeb indicating that creatine is most likely produced by cells. Ethylene thiourea (ETU) was found only in media containing mancozeb, and surprisingly, even in absence of cells. The amounts of ETU did not change in culture media of cells that do not metabolize the mancozeb demonstrating that the ETU found in these media was a degradation product present in the stock solution of mancozeb. In contrast, the amounts of ETU increased in the culture media of hepatocyte-like HepaRG cells exposed to mancozeb demonstrating the catabolism by these cells of this fungicide into its main metabolite.

For the 5 other metabolites of mancozeb (2-imidazoline, ethylene thiuram disulfide (ETD), ethylene thiuram monosulfide (ETM), ethylenethiourea-N-thiocarbamide (ETT) and Jaffe's base sulfoxide) for which it was not possible to obtain analytical standards, a full scan screening was realised and their mass were scrutinized. No peak with these exact masses were found in the samples, which confirmed their absence in the culture media of HepaRG cells incubated with mancozeb.

Identification of xanthine.

Incubation of mancozeb with hepatocyte-like HepaRG cells led to the production of two compounds detected by HPLC/UV at 247 nm at retention times of 2.7 and 4.5 minutes. The peak detected at 2.7 minutes co-eluted with ETU standard (data not shown) and was confirmed as ETU by UPLC-MS/MS.

To identify this compound, the first step was to determine its exact mass. To do this, the samples were injected onto an UPLC/MSMS with a Xevo-TQD ® triple quadrupole (Waters) in MRM (Multiple Reaction Monitoring) mode under analytical conditions similar to those used in HPLC in order to maintain a similar elution order of compounds and retention time.

The masses observed in positive electrospray ionization mode (153) and in negative ionization mode (151) led to the conclusion that the compound has a molecular mass of 152 g/mol. The use of the MASS BANK database (public mass spectrum library referencing about 10,000 compounds: <https://massbank.eu/MassBank/Search>) made it possible to identify two potential candidates: xanthine (CAS 69-89 -6) and oxypurinol (CAS 2465-59-0), two compounds of the purine family. We purchased the analytical standards (Tokyo Chemical Industry Co) of these two compounds (Oxypurinol - 95.1% / xanthine – 100 %) and their injection allowed the identification of the unknown compound: xanthine (Table 2).

The presence of xanthine was confirmed in the culture media of control cells unexposed to mancozeb at levels approximately 10 times lower than the amounts detected in media of cells incubated with 100 μ M mancozeb. Importantly, we found that exposure of HepaRG cells to 100 μ M MnCl₂ led to the production and release of xanthine in culture media in the same amounts as those found in cultures exposed to mancozeb demonstrating that xanthine was not a metabolite of mancozeb catabolism but a compound produced in response to both mancozeb and MnCl₂ treatment (**Figure 5, Table 1**).

Putative compounds based on molecular mass	CAS n°	Rt (min)	Cv (V)	Precursor ion	MRM1	MRM2	LOQ (μ M)
Xanthine	69-89-6	4.5	40	153	153>136 (24)	153>110 (16)	0.10
Oxypurinol	2465-59-0	5.0	40	153	153>80 (26)	153>136 (24)	0.50

Table 2 : Parameters for the identification of Xanthine and Oxypurinol in positive electrospray ionization mode (Rt: retention time; Cv: cone voltage; MRM1 quantification (uma) (collision energy - eV); MRM2 confirmation (uma) (collision energy - eV); LoQ: Limit of Quantification)

Considering the biosynthesis and catabolism of the xanthine, we decided to also analyze hypoxanthine and uric acid, two main compounds of this metabolic pathway. Analytical standard hypoxanthine (99.5%) were purchased from HPC standards and uric acid (100%) from Sigma-Aldrich and were injected to determine their retention time and their MS/MS parameters for identification and quantification. We also optimized the analytical method previously developed to quantify mancozeb, ETU, xanthine, hypoxanthine and uric acid (Table 3), by adjusting the elution parameters and cone voltage for the mass detector. An example of a chromatogram is shown in Figure 1. A mixture of water

and 0.1% NAH_4OH was the solvent for prepare a stock solution of xanthine and Dimethyl-sulfoxide (DMSO) for hypoxanthine.

We found that both xanthine and hypoxanthine were produced by hepatocyte-like HepaRG cells incubated with mancozeb but not uric acid. In addition, we evidenced that both xanthine and hypoxanthine were also produced upon exposure to MnCl_2 demonstrating that these compounds are not metabolites of mancozeb.

Compound	CAS n°	Rt (min)	CV(V)	Precursor ion	MRM1	MRM2	LOQ (μM)
ETU	96-45-7	2.1	30	103	103>44 (14)	103>60 (21)	0.1
Uric acid	69-93-2	2.5	40	169	169>70 (21)	169>141 (15)	0.1
Hypoxanthine	68-94-0	2.9	25	137	137>110 (19)	137>55 (25)	0.2
Xanthine	69-89-6	3.4	35	153	153>136 (24)	153>110 (16)	0.02
Mancozeb	8018-01-7	7.0	40	213	213>86 (25)	213>169 (17)	0.05

Table 3: Parameters for the identification of compounds, once xanthine has been identified, in positive electrospray ionization mode Rt: retention time; Cv: cone voltage; MRM1 quantification (uma) (collision energy - eV); MRM2 confirmation (uma) (collision energy - eV); LoQ: Limit of Quantification)

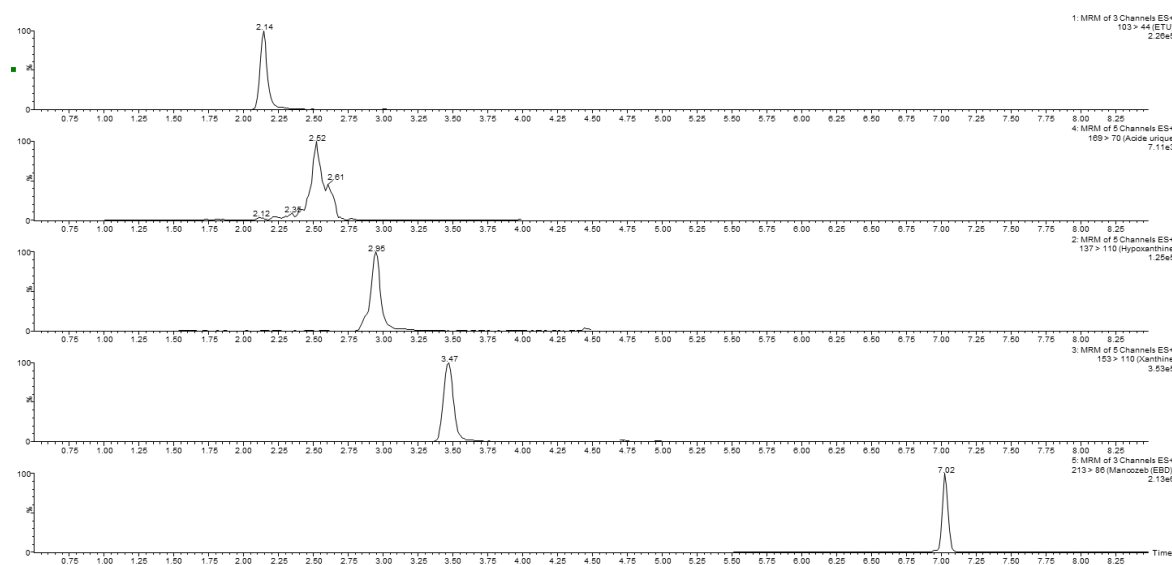
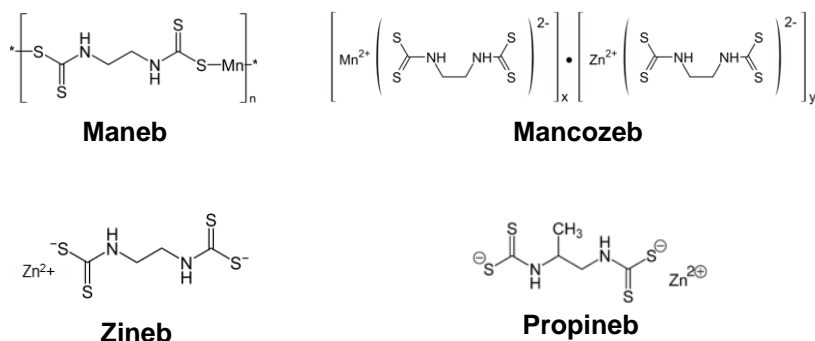


Figure 1 : Chromatogram obtained for an experimental sample (mancozeb 7 μM 3h) (ETU 1.2 μM ; uric acid 0.6 μM ; hypoxanthine 1.35 μM ; xanthine 1.2 ; mancozeb 57 μM).

Chemical structures of some DTCs.



DTCs share a chemical backbone ($\text{R}_2\text{NCS}_2\text{R}$). Some of them such as maneb, mancozeb, zineb and propineb are salts containing Mn^{2+} and/or Zn^{2+} . (Ajiboye et al., 2022).

References:

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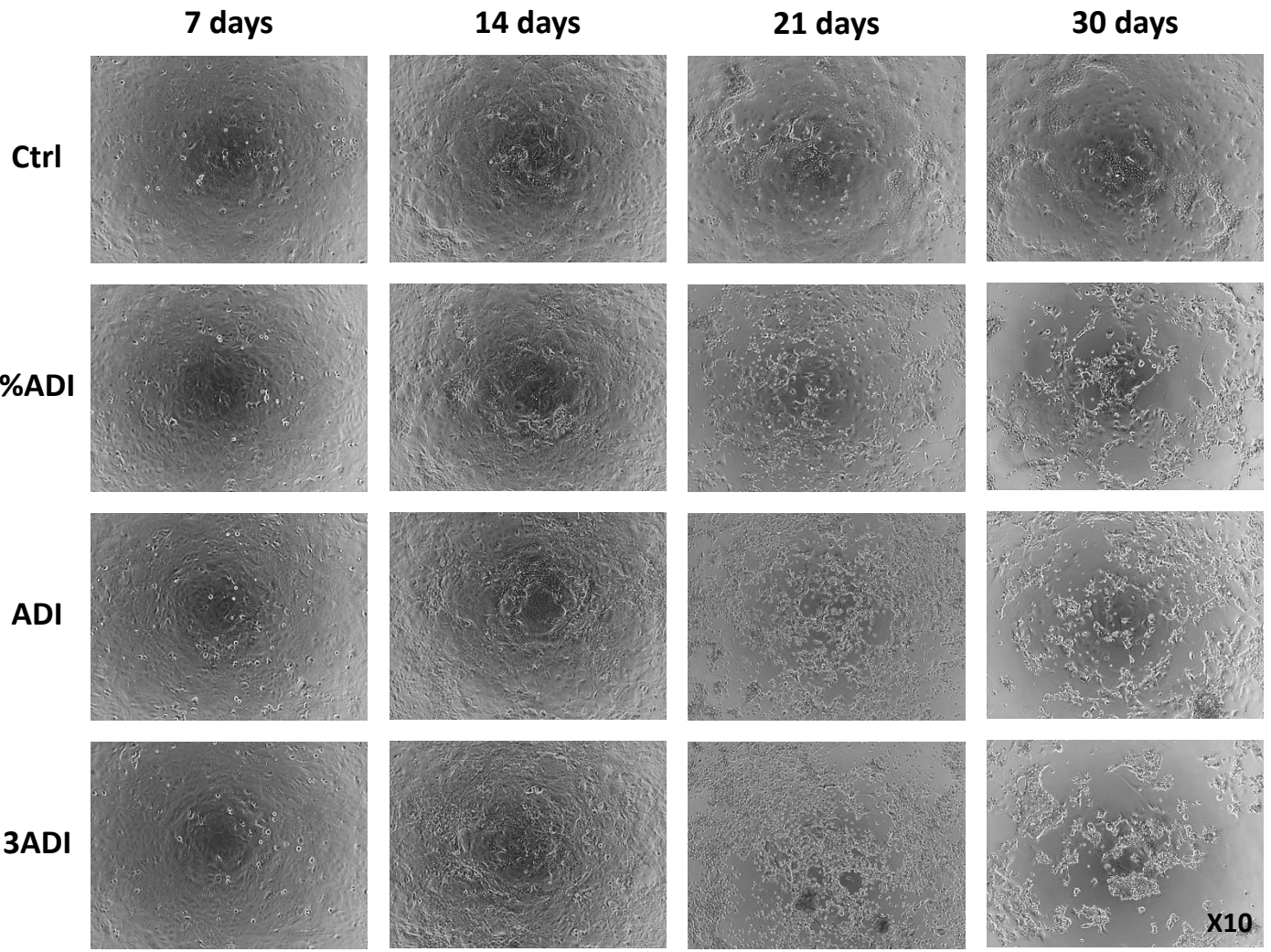
ENGST, R. & SCHNAAK, W. (1970a) [Studies on the metabolism of the ethylenebisdithiocarbamate fungicides maneb and zineb.] *Z. Lebensm. Unters. Forsch.*, **143**: 99-103

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Supporting Information 3.

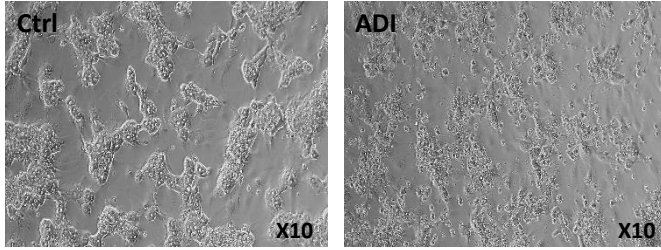
A

Differentiated HepaRG cells

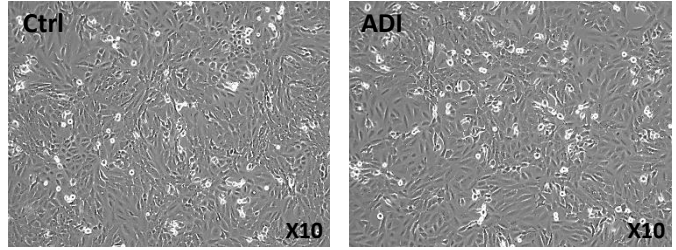


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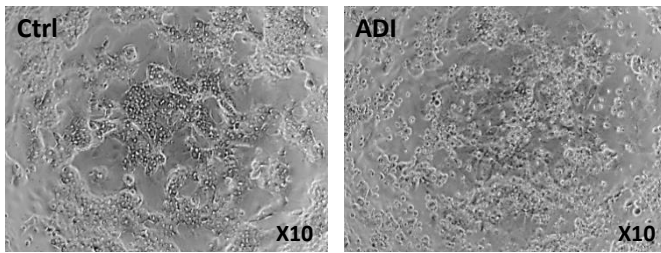
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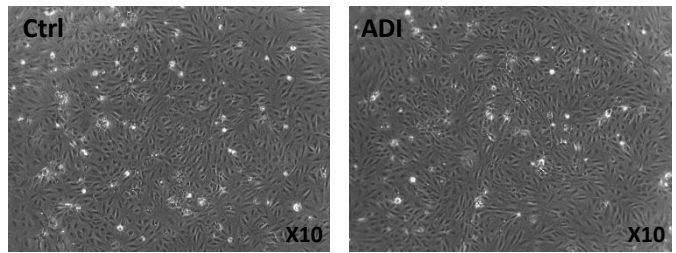
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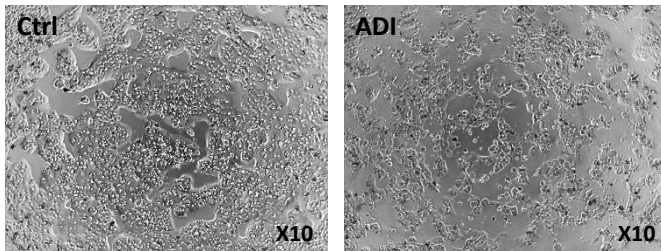
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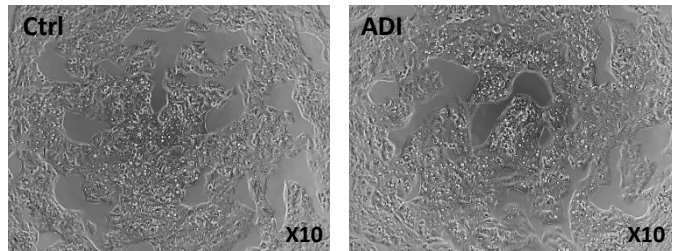
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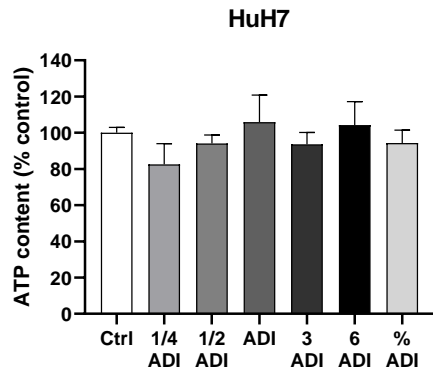
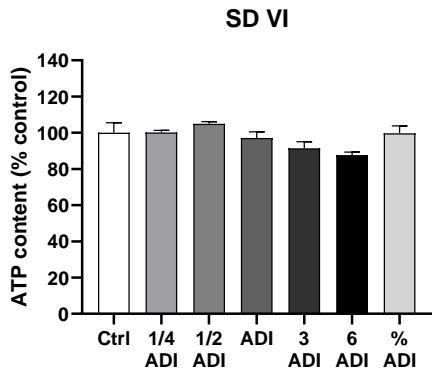
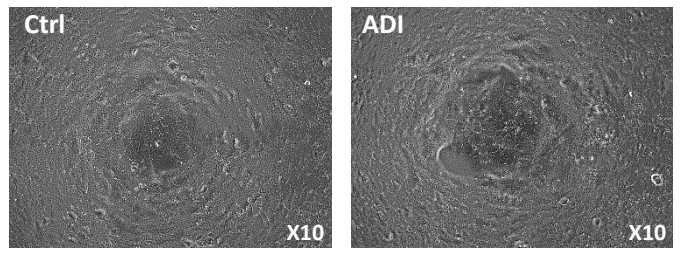
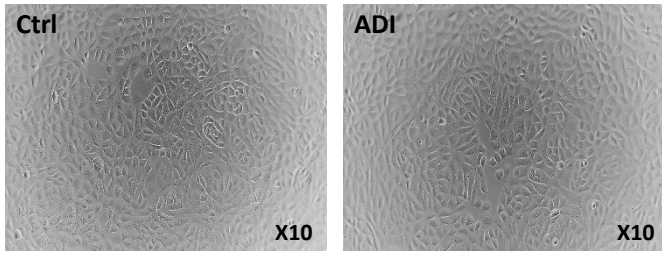
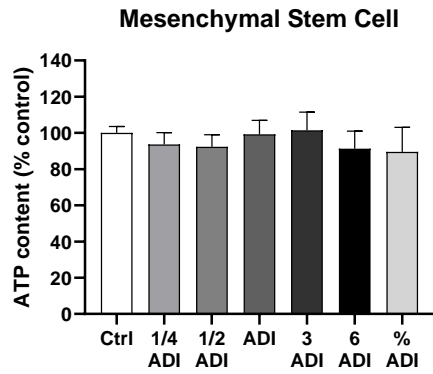
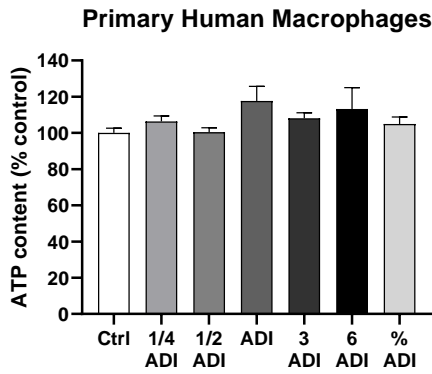
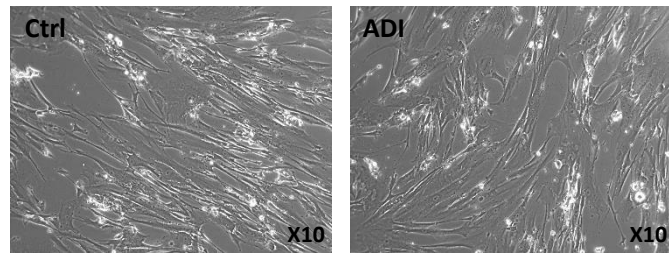
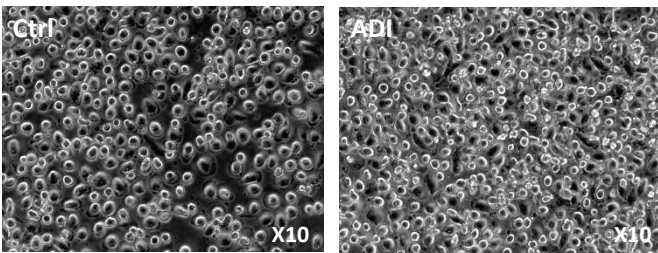


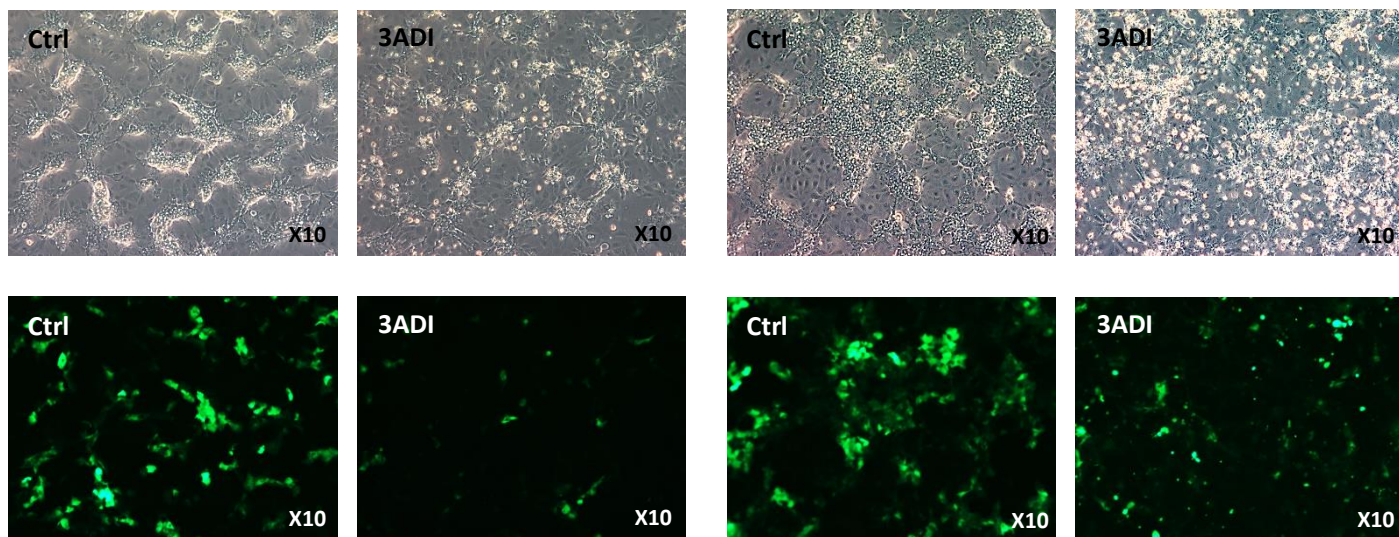
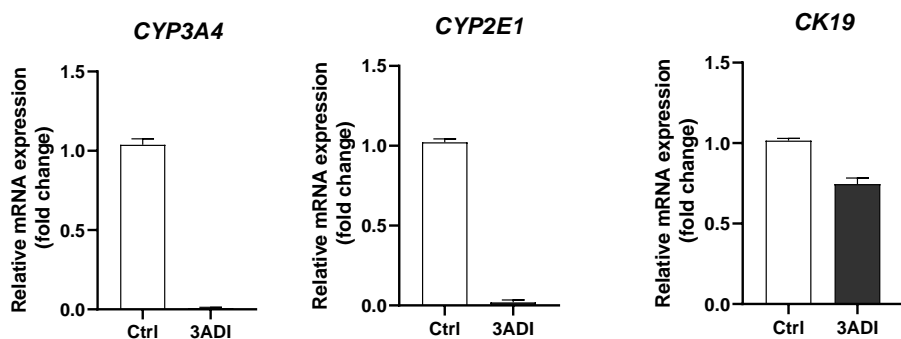
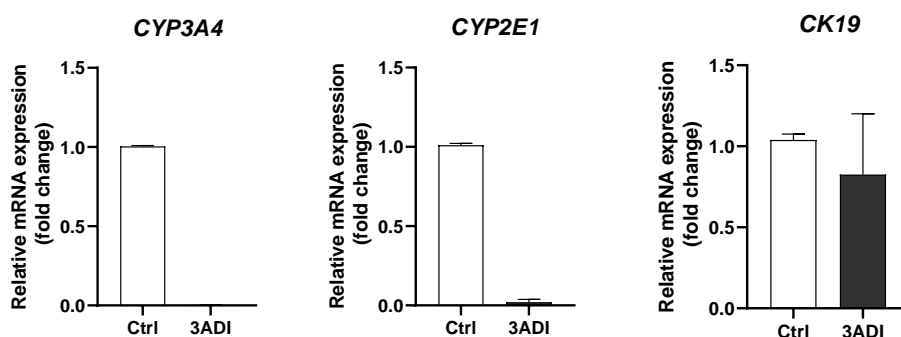
Primary Human Hepatocytes



HepG2



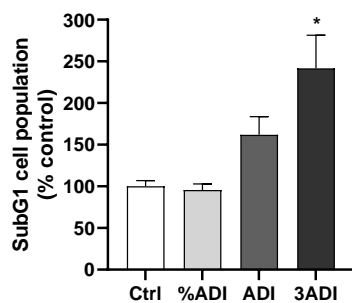
C**SD VI****HuH7****D****Primary Human Macrophages****Mesenchymal Stem Cell**

E**HepaRG CYP2B6****HepaRG CYP3A4****F****HepaRG CYP2B6****HepaRG CYP3A4****Supporting Information 3. Acute exposure of cell models to the pesticide mixture *in vitro*.**

Cell morphology in phase contrast microscopy of **A**) differentiated HepaRG cells treated with the pesticide mixture at different concentrations (%ADI, ADI or 3ADI) after 7, 14, 21 and 30 days of exposure, **B**) progenitor and differentiated HepaRG cells, human hepatocytes and HepG2 hepatoma cells in untreated condition (Ctrl) or after 48 hours of exposure with the pesticide mixture (ADI). **C**) Cell viability quantified by measuring the ATP content and cell morphologies in phase contrast microscopy in rat liver epithelial cells (RLC) SDVI and HepG2 human hepatoma cells, **D**) human macrophages and mesenchymal stem cells in untreated control cultures and after 48 hours of exposure to the pesticide mixture at different concentrations (1/4ADI, 1/2ADI, ADI, 3ADI, 6ADI or %ADI). Data were expressed as % of control. Results are means \pm SEM of at least 2 independent experiments. **E**) Cell morphology in phase contrast and GFP detection by fluorescence microscopy in HepaRG-CYP2B6prom-GFP and HepaRG-CYP3A4prom-GFP transgenic cells (Vlach et al., 2019) in untreated cultures (Ctrl) and after 48 hours of exposure to the pesticide mixture (3ADI). **F**) Relative expression of *CYP3A4*, *CYP2E1* and *cytokeratin 19* (*CK19*) mRNA levels in untreated control (Ctrl) and pesticide-treated HepaRG-CYP2B6 and HepaRG-CYP3A4 cells.

Supporting Information 4.

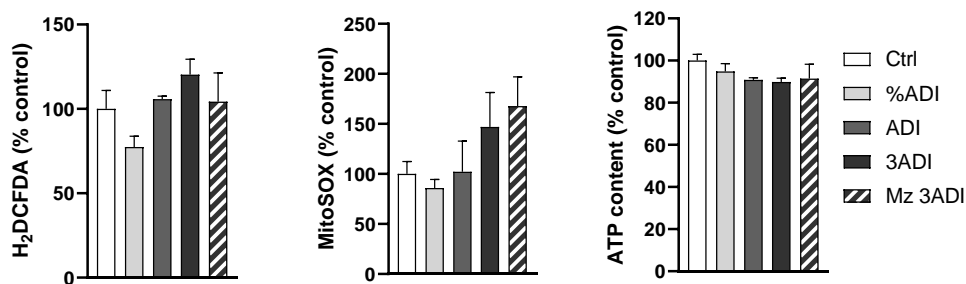
A



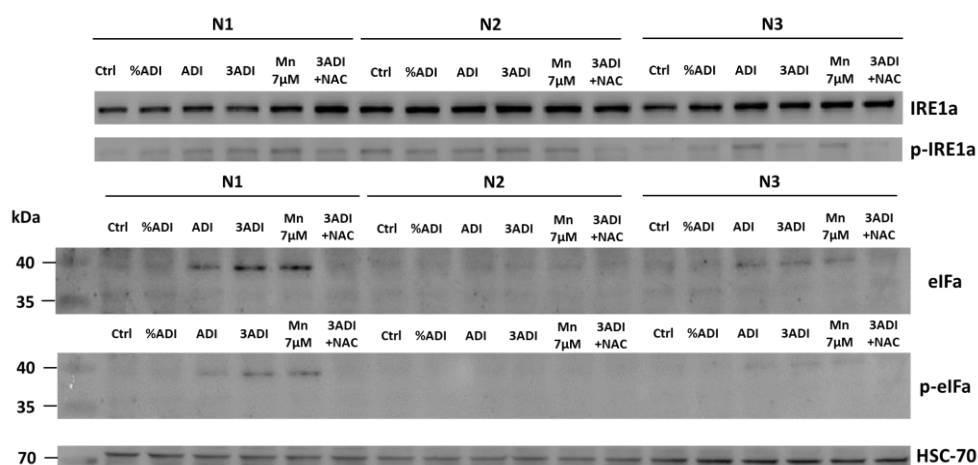
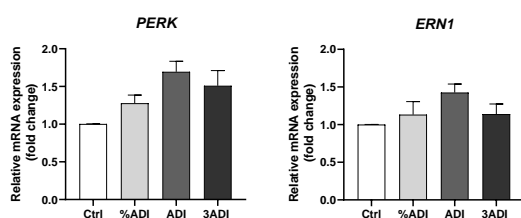
B

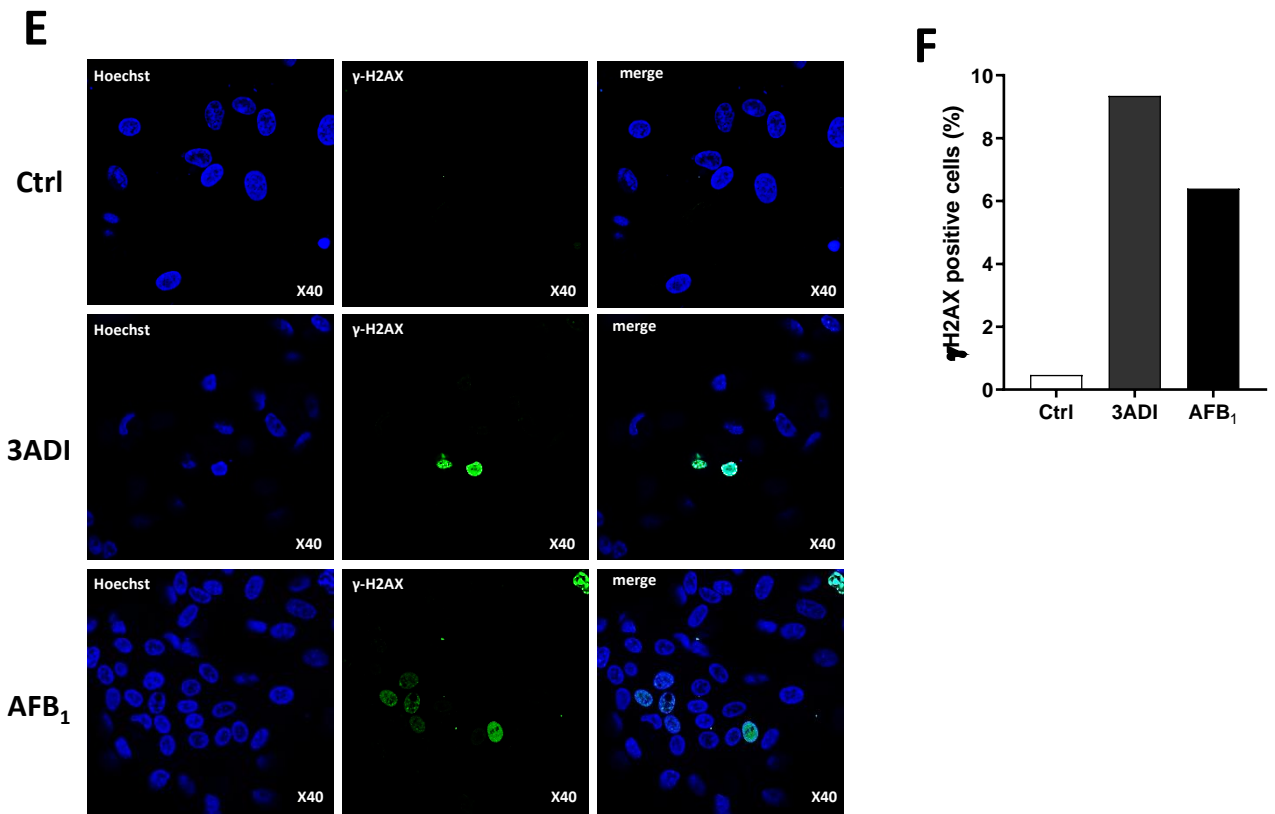
	I/CS	II/CS	III/CS	IV/CS	V/CS
Ctrl	0.33 ± 0.02	0.45 ± 0.05	0.44 ± 0.06	1.66 ± 0.35	0.95 ± 0.24
Maneb 6ADI	0.35 ± 0.07	0.45 ± 0.05	0.42 ± 0.12	1.70 ± 0.24	1.04 ± 0.09
MnCl ₂ 14μM	0.30 ± 0.08	0.41 ± 0.10	0.45 ± 0.07	1.73 ± 0.11	0.85 ± 0.14

C



D





Supporting Information 4. Apoptosis and genotoxicity in HepaRG cells and human hepatocytes exposed to the pesticide mixture. **A.** Percentages of apoptotic HepaRG cells estimated through the quantification of SubG1 population by flow cytometry after exposure to the pesticide mixture for 24h. DNA was stained using propidium iodide. **B.** Activity of the mitochondrial complexes I to V in control culture and in cells exposed to maneb and no significant differences in enzymatic activities could be observed between untreated and pesticide-exposed cells. Enzymes activities of all complex were expressed as nmol substrate/min/10⁶cells using the Beer Lambert's law and were normalized to the citrate synthase activity (N=3). **C.** ROS production was evaluated using H₂DCFDA and MitoSOX probes and cell viability was evaluated by quantification of the relative ATP contents in cholangiocyte-like HepaRG cells exposed for 24h to the pesticide mixture (%ADI, ADI or 3ADI) or mancozeb alone (Mz 3ADI). Data were normalized to the untreated control culture (Ctrl). Results are means ± SEM (N≥3), *p< 0.05 significantly different from control (Ctrl). **D.** Relative mRNA levels of *PERK* and *ERN1* (upper charts) and western blot analysis of IRE1α phosphorylation and eIF1α protein expression in hepatocyte-like HepaRG cells (N=3). **E.** Detection of γ-H2AX positive HepaRG cells by fluorescence microscopy in untreated cells (Ctrl) and exposure to the pesticide mixture for 16h (3ADI). Aflatoxin B₁ (24h, 0,25μM) was used as genotoxic positive control (AFB₁). **F.** Quantification of γ-H2AX positive cells versus total nuclei (Hoechst staining) using Image J. Results are means of at least 3 independent experiments (N≥3).

Table Quantities (ng/well) \pm SEM of manganese and zinc by ICP-MS

		Intracellular			Mitochondria		
		Hepatocytes	Cholangiocytes	Progenitors	Hepatocytes	Cholangiocytes	Progenitors
Manganese (ng/well)	Ctrl	12.14 \pm 0.43	1.72 \pm 0.41	1.23 \pm 0.10	0.73 \pm 0.10	0.46 \pm 0.04	0.26 \pm 0.00
	Ctrl + ZnCl ₂ 70 μ M	14.13 \pm 4.34			0.85 \pm 0.04		
	MnCl ₂ 7 μ M	65.20 \pm 15.37	6.19 \pm 1.98	3.06 \pm 0.39	7.43 \pm 2.39	0.77 \pm 0.08	0.37 \pm 0.02
	MnCl ₂ 7 μ M + ZnCl ₂ 70 μ M	39.78 \pm 1.99			3.34 \pm 0.78		
	Maneb 3ADI	55.47 \pm 8.28	4.85 \pm 0.69	3.51 \pm 0.28	11.03 \pm 7.06	0.81 \pm 0.19	0.46 \pm 0.07
	Maneb 3ADI + ZnCl ₂ 70 μ M	39.28 \pm 1.85			3.94 \pm 1.33		
Zinc (ng/well)	Ctrl	122.05 \pm 12.78	26.76 \pm 4.81	30.20 \pm 1.44	13.02 \pm 3.27	5.04 \pm 1.83	2.86 \pm 0.87
	Ctrl + ZnCl ₂ 70 μ M	140.21 \pm 3.08			4.18 \pm 0.79		
	MnCl ₂ 7 μ M	74.55 \pm 11.70	43.11 \pm 13.96	29.44 \pm 0.89	8.70 \pm 2.68	9.73 \pm 4.08	2.03 \pm 0.20
	MnCl ₂ 7 μ M + ZnCl ₂ 70 μ M	110.96 \pm 18.75			5.17 \pm 0.90		
	Maneb 3ADI	71.36 \pm 6.66	23.19 \pm 3.51	31.48 \pm 2.37	12.10 \pm 4.54	4.11 \pm 1.06	4.33 \pm 1.35
		Maneb 3ADI + ZnCl ₂ 70 μ M	111.45 \pm 12.09			6.55 \pm 1.72	

Supporting Information 5. Quantification of Mn and Zn in HepaRG cells by ICP-MS. Results expressed in ng of metals/culture wells are means of at least 3 independent experiments (N \geq 3).