Role of Genetic Toxicology in Environmental Public Health: Lessons Learnt from E- wastes and Nanoparticles in Nigeria

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What is an Environment?

- It is the surroundings or conditions in which a person, animal or plants lives or operates.

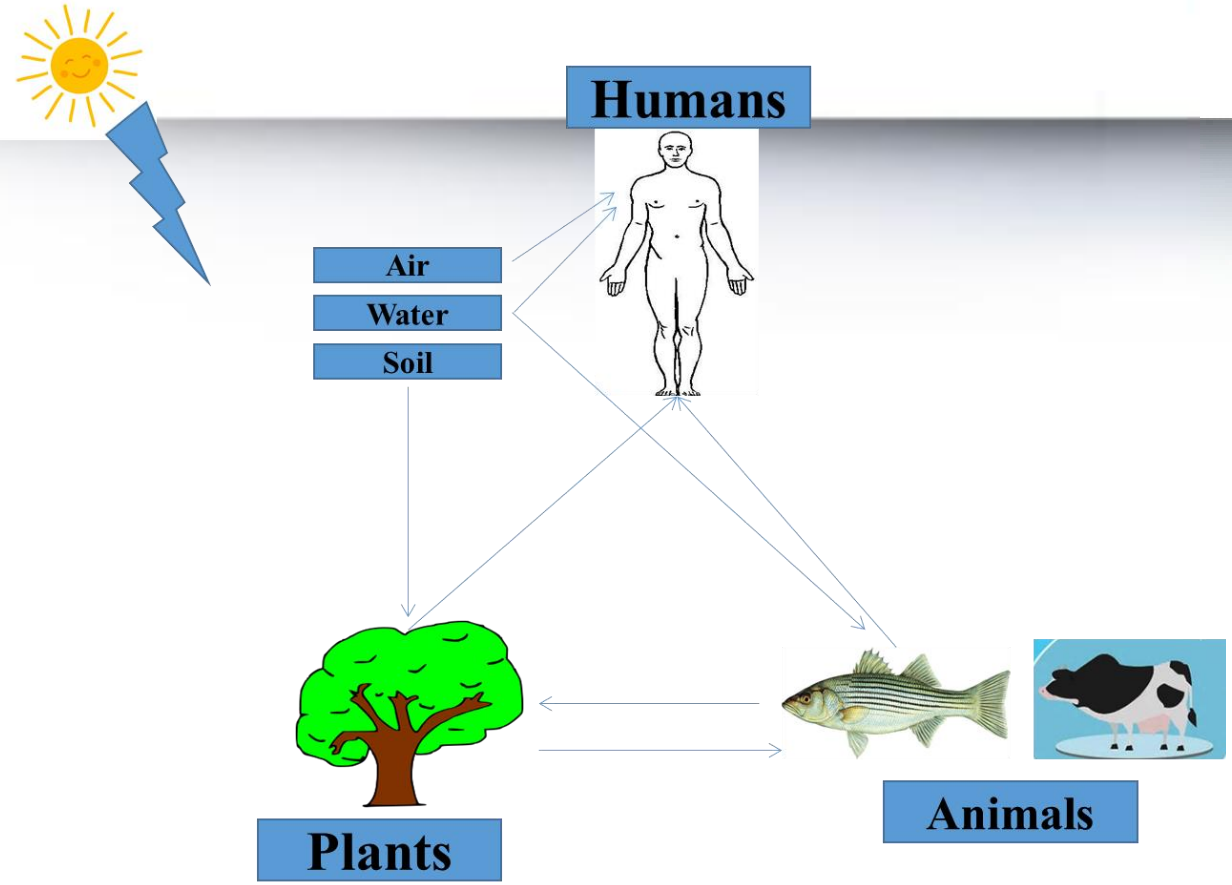

Fig. 1: Interactions in the Environment

Fig. 2: SDGs targeting Sustainable Environment >>>>>>>>

What is Genetic Toxicology?

- It is a branch of Toxicology that deals with the adverse effects of physical, chemical and biological agents on the genetic material (DNA).

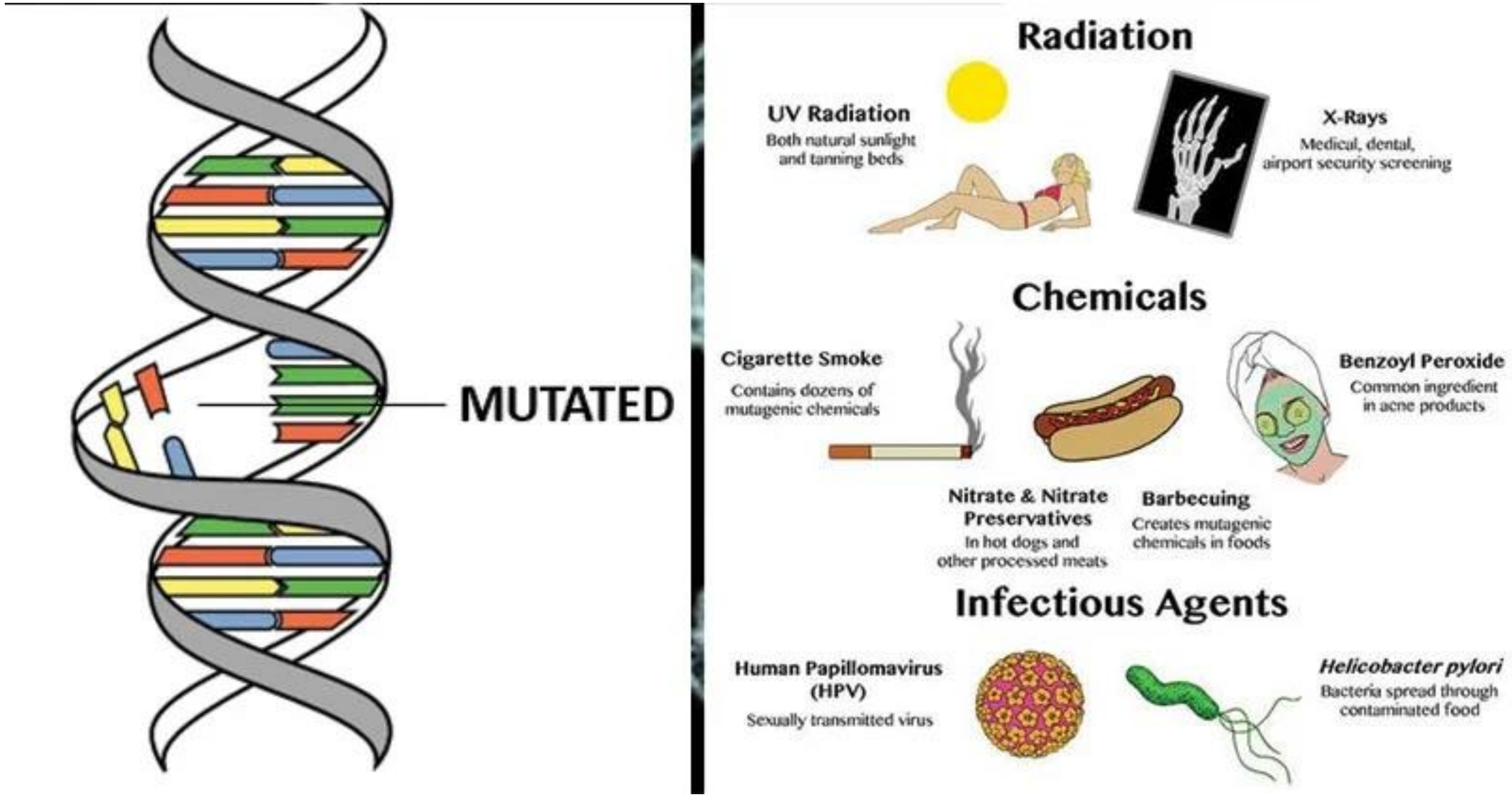

Fig. 3: Agents of Genetic damage (Ren *et al*., 2017)

Some Genetic Toxicology assays

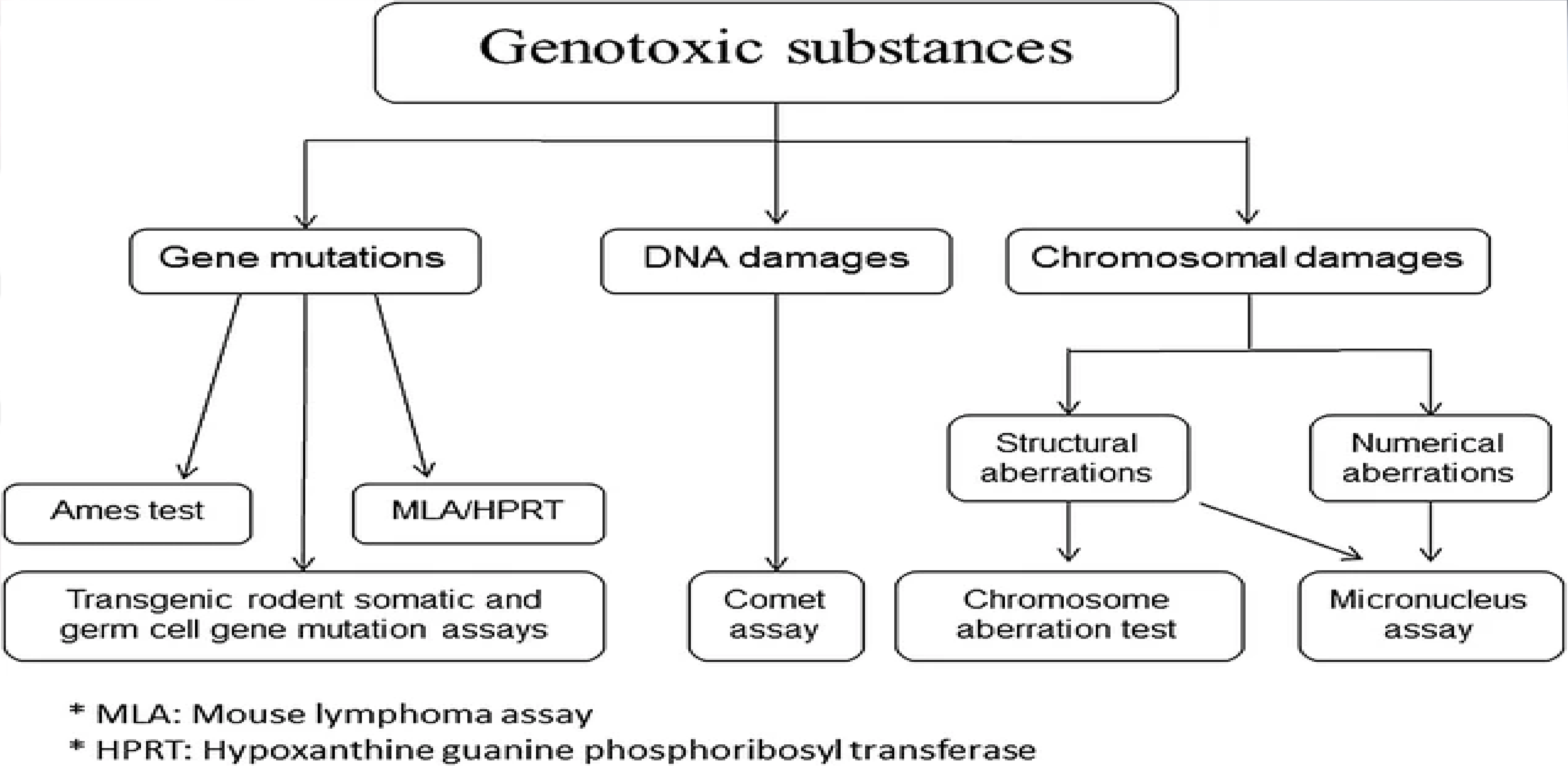

Fig. 4: Types of Genotoxic Damage and Some Gentox Assays (Ren *et al.*, 2017)

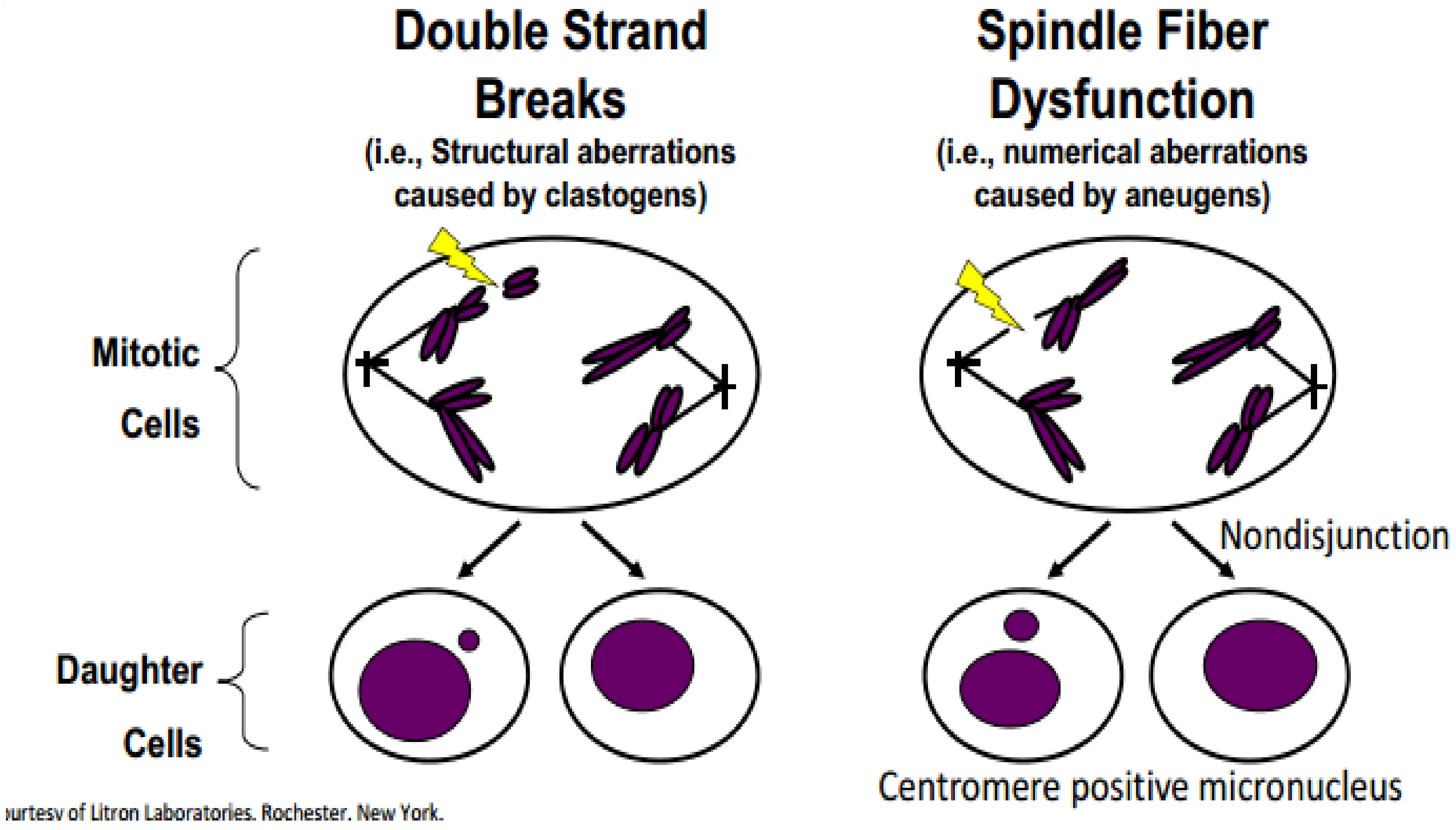

Fig. 5: Cytogenetic damage and formation of micronucleus (White, 2017)

Environmental pollution in Nigeria

- **How much do we know about emerging contaminants in Nigeria?**

  - **Electronic waste (E-waste)**

  - **Nanoparticles**

Electronic waste (E-waste)

- Obsolete materials that have reached its end – of – life (EoL) by original users or no longer needed.

- Nigeria received 288 000 tonnes of e- wastes in 2018

Fig.6 : A. Used Electrical Electronic equipment on display (Amachree, 2013) B. Informal recycling and burning activities C - E. improper disposal of e- waste on open dumpsite at Alaba International Electronics Market Lagos F. Lidless well (Ogunsuyi, 2012)

Challenges **2013**, *4*, 169-187; doi:10.3390/challe4020169

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Article

In Vivo Cytogenotoxicity and Oxidative Stress Induced by Electronic Waste Leachate and Contaminated Well Water

Adekunle A. Bakare [1,*], Okunola A. Alabi [1,2], Adeyinka M. Gbadebo [3], Olusegun I. Ogunsuyi [1] and Chibuisi G. Alimba [1]

- **There was significant ($p < 0.05$) inhibition of root growth and mitosis in *Allium cepa*.**
- **Cytological aberrations such as spindle disturbance, C-mitosis and binucleated cells, and morphological alterations like tumor and twisting roots were also induced.**
- **There was concentration-dependent, significant ($p < 0.05$) induction of micronucleated erythrocytes and nuclear abnormalities such as blebbed nuclei and binucleated erythrocytes in C. gariepinus.**
- **A significant increase ($p < 0.001$) in CAT, GSH and MDA with concomitant decrease in SOD concentrations were observed in the treated mice.**
- **Pb, As, Cu, Cr, and Cd analyzed in the tested samples contributed significantly to these observations.**
- **The well water samples and leachate contained substances capable of inducing somatic mutation and oxidative stress in living cells**

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Figure 2. Macroscopic effects induced in *Allium cepa* exposed to e-waste leachate. (**a**) Normal root growth in the control group, (**b**) short, scanty, swollen (tumour) roots with blackened root tips and rottenness at the basal plate, (**c**) short, scanty and blackened root length (**d**) short, backward bending to spiralling roots with blackened/yellowish root tips.

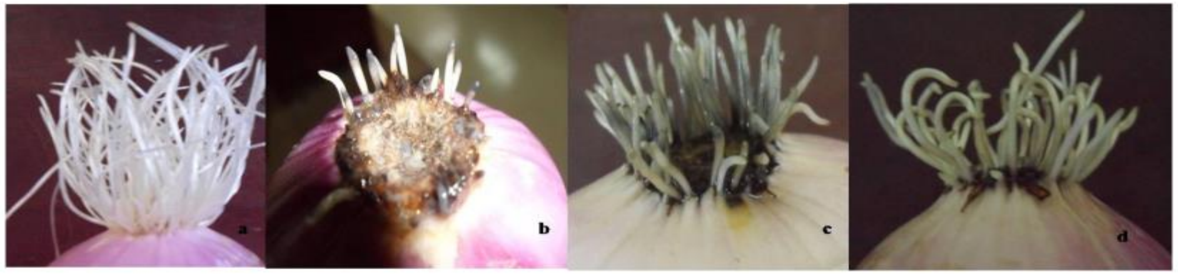


Figure 5. Normal erythrocyte (N), micronucleated erythrocytes (M), binucleated cell (BN) and blebbed nuclei (BL) in *Clarias gariepinus* exposed to electronic waste leachate and contaminated well water (×1000).

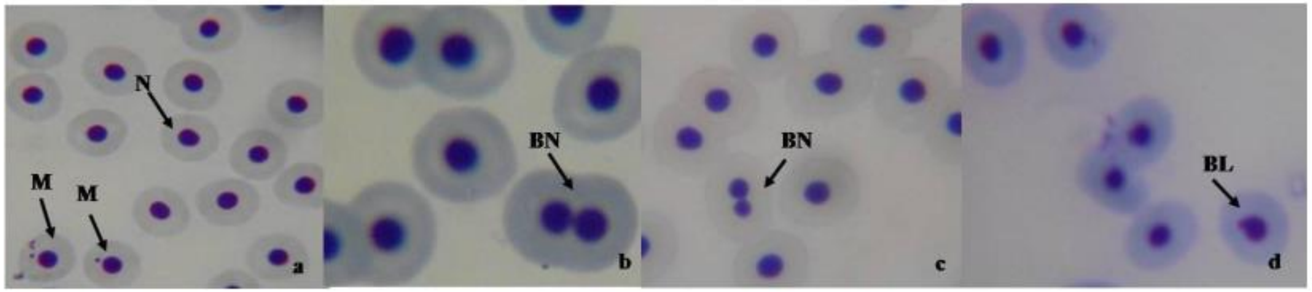
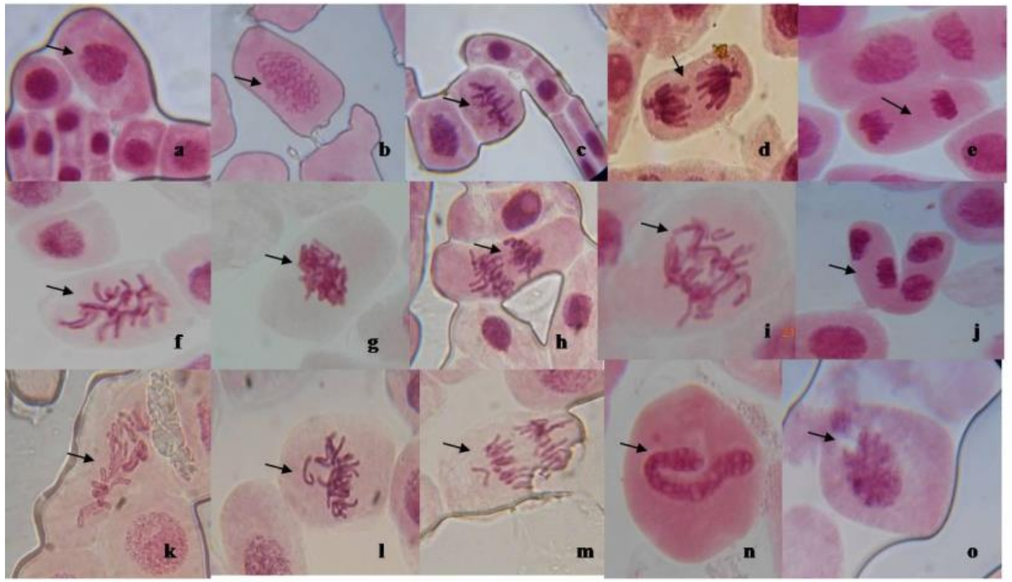


Figure 4. Aberrations observed in *Allium cepa* root tip cells exposed to e-waste leachate and well waters. (**a–e**) Normal cells at Interphase (a), prophase (b), metaphase (c), anaphase (d) and telophase (e); (**f**) Spindle disturbance at metaphase; (**g,h**) stickiness at metaphase (g) and anaphase (h); (**i**) Bridges and non-disjunction at anaphase; (**j**) polar deviations at telophase; (**k**) C-mitosis; (**l**) vagrant and fragment chromosomes at metaphase; (**m**) vagrant chromosome at anaphase; (**n,o**) Nuclear abnormalities (NA) with nuclear point (n) and broken nuclear material (o) (×1000).



Nanoparticles

- **Nanoparticles (NPs) can be defined as particles having one or more dimensional feature within 1 and 100 nm (Sadek *et al.*, 2016).**

- **NPs exist in one of the two forms: naturally occurring nanoparticles and engineered nanoparticles (Figure 7) (Kumar *et al.*, 2014).**

EXAMPLES OF NATURALLY OCCURING AND ANTHROPOGENIC SOURCES OF NANOPARTICLES

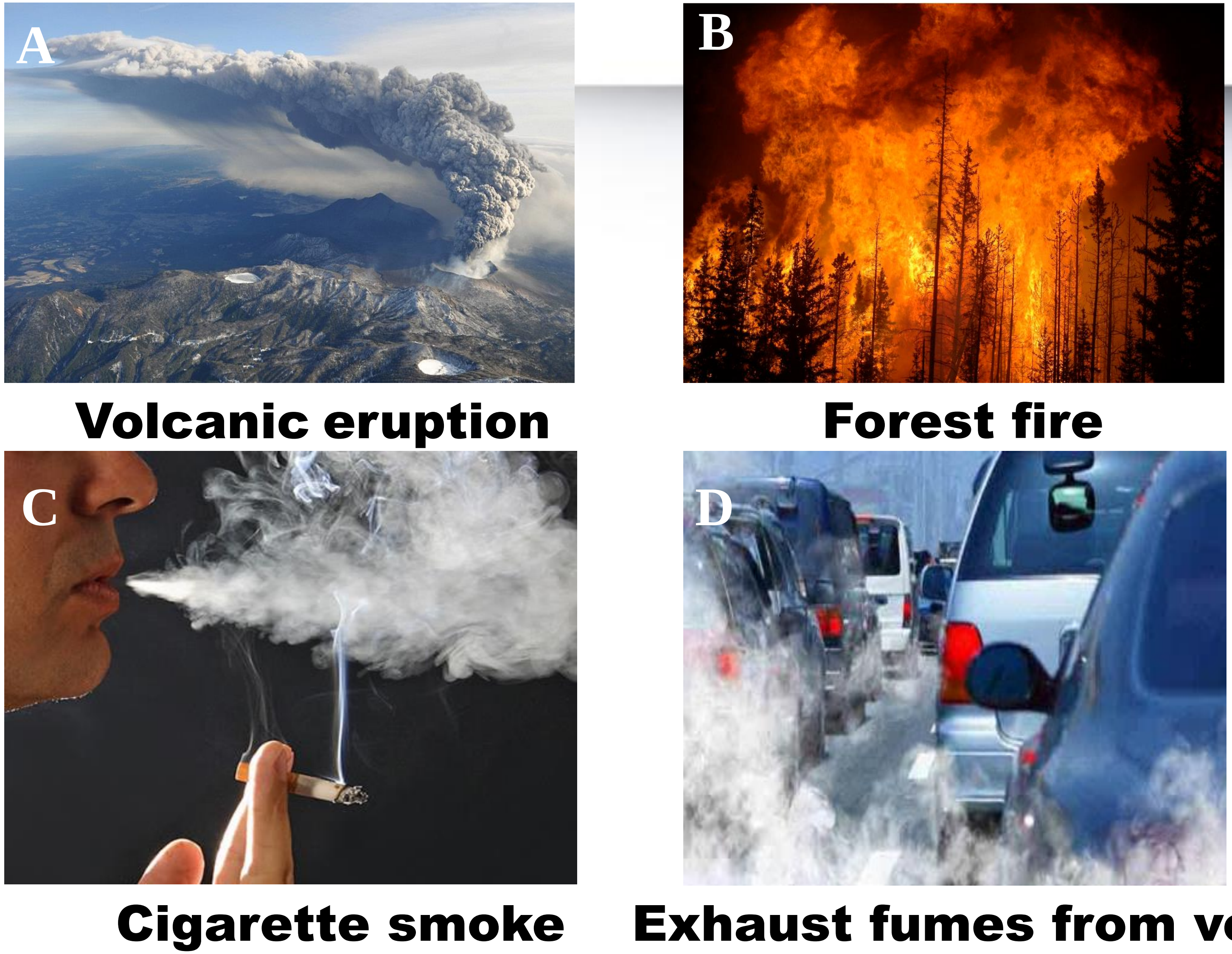


Fig. 7: Examples of naturally occurring events that contain nanoparticles. (A) and (B). Examples of anthropogenic events that contain nanoparticles. (C) and (D).

PROPERTIES OF NANOPARTICLES

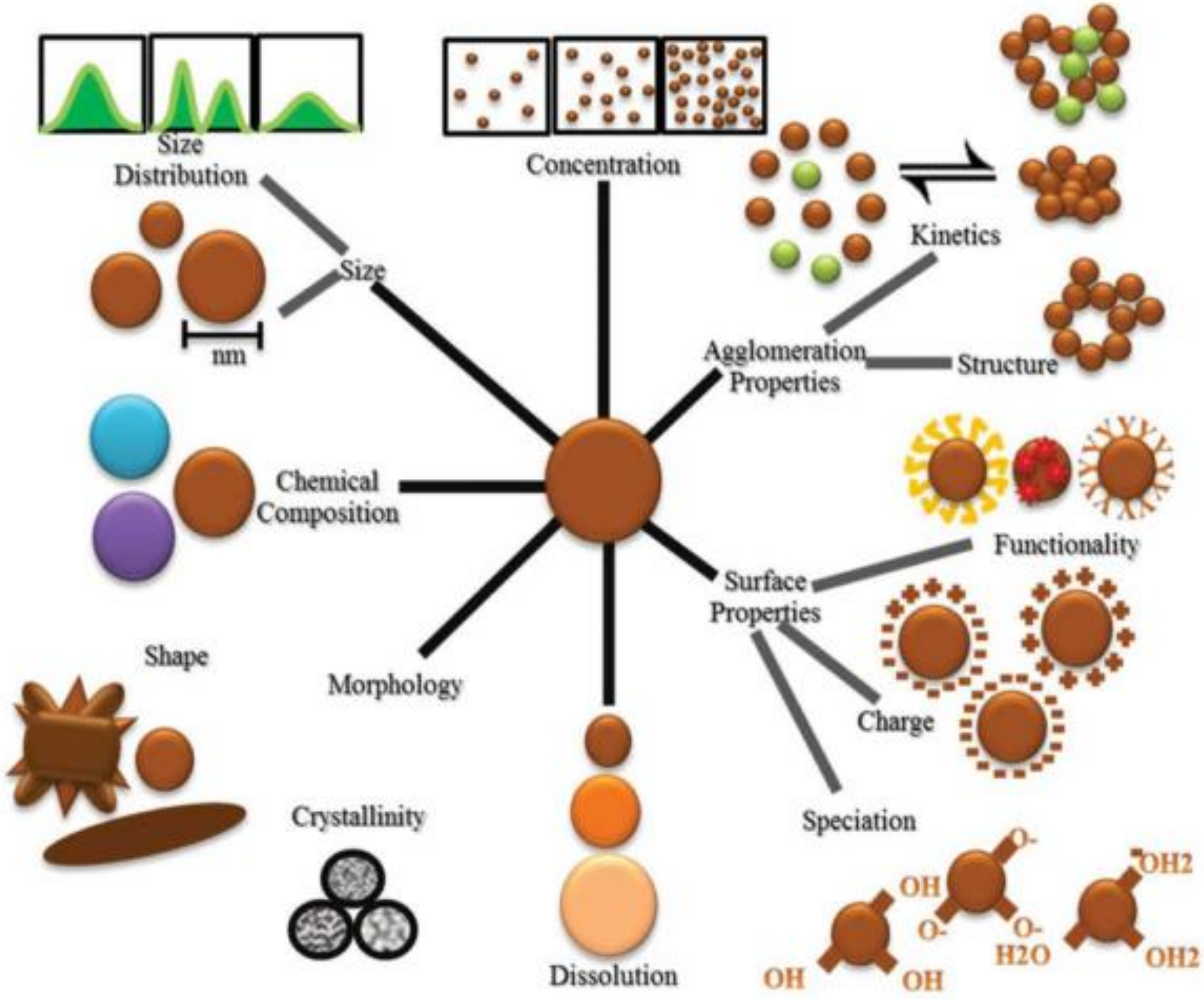


Fig. 8: Physiochemical properties of nanoparticles. Source: Koedrith *et al.* (2014).

CLASSIFICATION OF NANOMATERIALS BASED ON THEIR CHEMICAL COMPOSITION

NANOMATERIALS

Metal oxides
- Titanium dioxide (TiO_2)
- Zinc oxide (ZnO)
- Copper oxide (CuO)
- Silica (SiO_2)
- Iron oxide (Fe_2O_3, Fe_3O_4)
- Manganese oxide (MnO_2)

Metals
- Gold (Au)
- Silver (Ag)
- Cobalt (Co)
- Nickel (Ni)

Quantum dots
- Cadmium
- Selenium

Carbon nanotubes
- Single walled (SWNT)
- Multi walled (MWCNT)
- Fullerene derivatives

TABLE 1: APPLICATIONS OF SOME NANOPARTICLES

NANOPARTICLES	USES
Titanium dioxide	Cosmetics, sunscreens, toothpastes, inks, plastics, papers, pharmaceuticals, photocatalysts and anticorrosive.
Zinc oxide	Cosmetics, sunscreens, fungicides, anticancer drugs, food additives, catalysts and foot deodorant.
Ag	Water treatment, fabric softener, wound dressing, kitchen utensils, computer keyboards, baby products, contraceptives and toothpaste.
Copper oxide/Copper	Paints, plastics, lubrication oil additive, conductive coatings, printer inks, 'anti-ageing' cream and skin conditioner.

- **Titanium dioxide (TiO_2) and zinc oxide (ZnO) nanoparticles are one of the most utilised metal oxide NPs.**

- **TiO_2 NPs are referred to as titanium (IV) oxide, titania anhydride or Ti white.**

- **Are white, odourless, and non-combustible pigments.**

- **Possess photocatalytic and anticorrosive properties (Sadiq *et al*., 2012).**

- **Exist in one of three forms: rutile, anatase and brookite.**

- **Rutile and anatase are the most important forms in relation to the use of TiO_2 in consumer products (Chen *et al*., 2014).**

- **Account for over 70% of the total production volume of NPs worldwide (Shi *et al*., 2013).**

- **ZnO NPs are known as oxydatum, zinci oxicum, permanent white, ketozinc and oxozinc.**

- **They possess antimicrobial, antifungal and UV filtering properties (Gerloff *et al*., 2009).**

- **ZnO NPs have two main forms: the wurtzite and zinc blende structures.**

- **They have received great attention because of the putative anticancer, drug delivery and biomedical imaging properties (Sharma *et al*., 2011).**

- **More than 300 companies around the world are producing excess 1.2 million tons of ZnO NPs per year, making it the third highest producing metal oxide NP (Kumar *et al*., 2014).**

- **Silver nanoparticles (Ag NPs) known as nanosilver possess antimicrobial property among other properties (Gee *et al*., 2014).**

- **They are used for medical, food, health care, consumer, and industrial purposes (Zhang *et al*., 2016).**

- **They are the most frequently used of all nanomaterials constituting 24% of all the products (Vance *et al*., 2015).**

- **About 550 tons of Ag NPs are produced annually (Bondarenko *et al*., 2013).**

- **Copper oxide nanoparticles (CuO NPs) are also known as cupric oxide nanopowder and possess excellent thermophysical and antimicrobial properties.**

- **They have biocidal properties and are utilised in many biomedical applications (Grigore *et al.*, 2016).**

- **Over 200 tons of CuO NPs are produced annually (Keller et *al.*, 2013).**

Fig. 9: Examples of consumer products that contain TiO_2 NPs, ZnO NPs, Ag NPs and CuO NPs.

- **The production of metal and metal oxide NPs is estimated to significantly increase to 1 663 168 tons by 2020 (Future Market Inc., 2013).**

- **Due to the numerous applications of these NPs in consumer products, the chances of human and environmental exposures may exponentially increase.**

- **Humans get exposed to NPs at various steps through:**
  - **industrial (manufacturing, processing and packaging)**
  - **use (consumer products, devices, medicines, etc.)**
  - **environment (contaminated water, aerosolised particles and disposal. (Figure 10)**

EXPOSURE ROUTES OF NANOPARTICLES

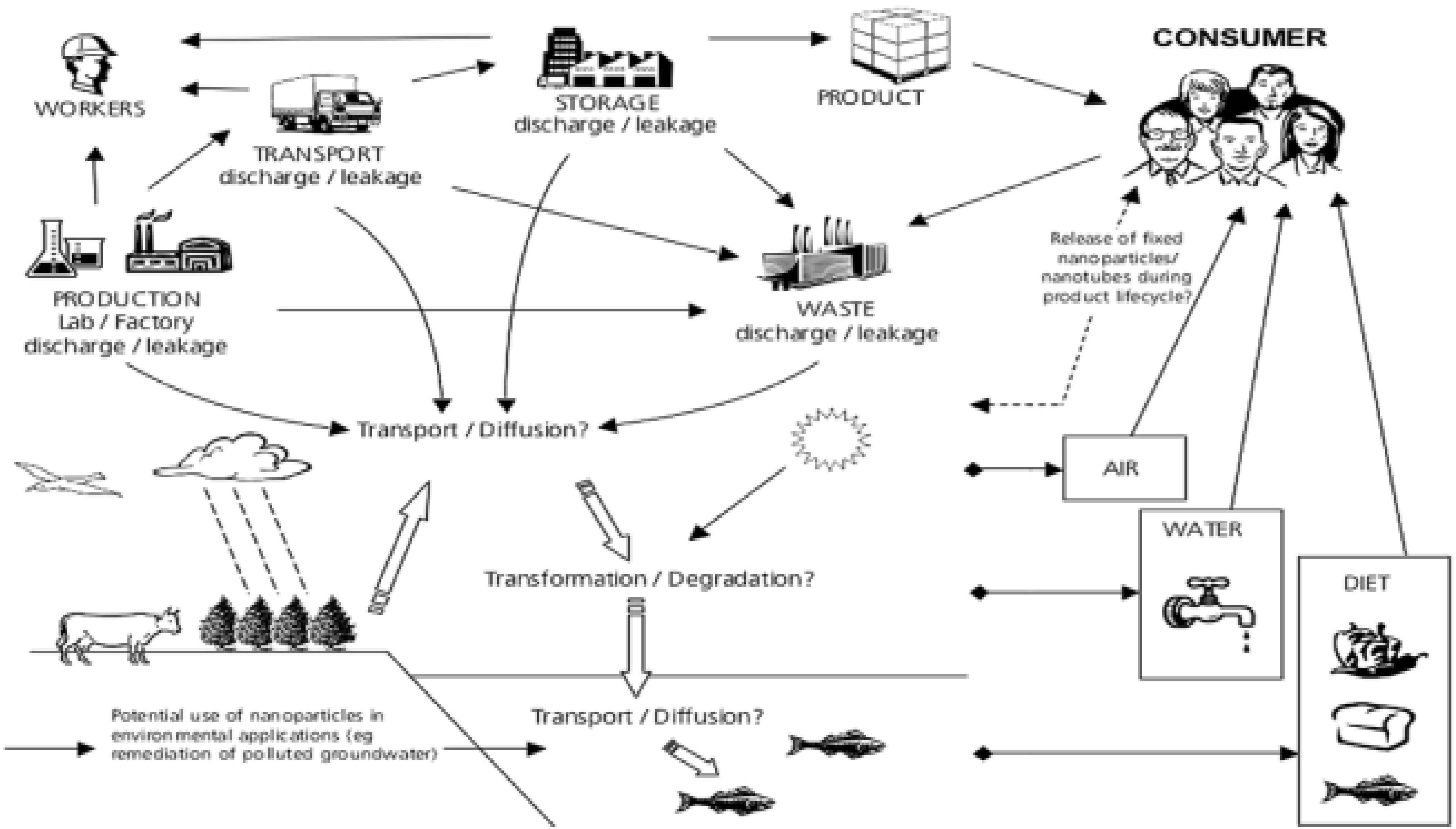


Fig. 10: **Potential release, exposure, and uptake of NPs in the ecosystem. Royal Society of London, 2004.**

JUSTIFICATION

- **Increase in the manufacturing and use of TiO_2, ZnO, Ag and CuO NPs has raised concerns about their safety for public health.**

- **Pollution risk is eminent and should not be ignored as Nigeria is still at the infancy stage of nanotoxicological research.**

- **Culmination of waste disposal that contain individual forms of these NPs may form heterogeneous aggregates in the environment.**

- **Short or long term genotoxic consequences on the biota due to the interactive effects of these individual NPs.**

- **More *in vitro* genotoxicity studies on the individual NPs with no existing *in vivo* genotoxicity studies on the mixtures of these individual NPs.**

- **Interaction of these individual NPs in the biological system may elicit immune responses, absorption of physiological barriers and interaction with DNA repair processes.**

AIM

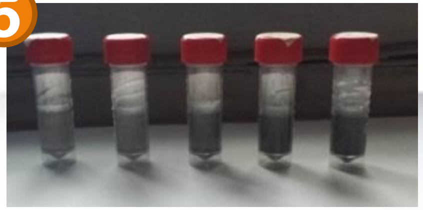
To investigate the potential DNA damaging effect of the individual NPs (TiO_2, ZnO, Ag and CuO) and their mixtures (TiO_2 + ZnO; Ag + CuO) in:

Allium cepa

Clarias gariepinus

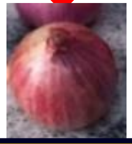
Mus musculus

Methodology

1. Ethical approval by ACUREC, UI
2. AgNPs, CuONPs and 1:1 mixture
3. 10 mins sonication
4. 5 mins vortexing
5. 

5 Sub lethal concentrations

6. Physicochemical characterisation
   - Morphologies of AgNPs and CuONPs (Georgantzopoulou *et al.* 2016) .
   - Particle size distribution, zeta (ζ) potential and polydispersity index (Cambier *et al.*, 2018)



7 Onion bulbs

- *Allium cepa* assay (Fiskesjo, 1985; Oyeyemi and Bakare, 2013)
- 8 bulbs/ concentration (5-80 mg/L)
- 24 h exposure and recovery periods

8 Juveniles of *C. gariepinus*

- 96 h Acute toxicity (OECD TG 203)
- 5 fish/ concentration (6.25 – 100mg/L); 7 and 28 days
- Piscine Micronucleus assay (Bakare *et al.*, 2013)
- Haematological analysis; Histopathological analysis (skin, gill and liver) ;Hepatic oxidative stress analysis (MDA,, GSH, CAT and SOD)

9 Male Swiss albino mice

- Acute toxicity (OECD TG 420)
- Micronucleus (Schmid 1975; Bakare *et al.*, 2009) & Sperm morphology assays
- Haematological analysis; Histopathological analysis of liver;
- Serum hepatic injury biomarkers (ALT and AST);
- Hepatic oxidative stress analysis (MDA, GSH, CAT and SOD)
- Hormonal assays

Environmental Science and Pollution Research
https://doi.org/10.1007/s11356-019-05958-6

RESEARCH ARTICLE

Check for updates

Genetic and systemic toxicity induced by silver and copper oxide nanoparticles, and their mixture in *Clarias gariepinus* (Burchell, 1822)

Olusegun I. Ogunsuyi[1] · Opeoluwa M. Fadoju[1] · Olubukola O. Akanni[2] · Okunola A. Alabi[3] · Chibuisi G. Alimba[1] · Sebastien Cambier[4] · Santhana Eswara[5] · Arno C. Gutleb[4] · Oluwatosin A. Adaramoye[2] · Adekunle A. Bakare[1]

Received: 17 December 2018 / Accepted: 11 July 2019

- **Both NPs and their mixture induced significant ($p < 0.05$) increase in MN frequency and other nuclear abnormalities.**

- **There was significant decrease in haemoglobin concentration, red and white blood cell counts.**

- **Histopathological lesions observed include epidermal skin cells and gill lamellae hyperplasia and necrosis of hepatocytes.**

- **The levels of MDA, GSH and activities of SOD and CAT were impacted in C. gariepinus liver following the exposure to the NPs and their mixture.**

- **Interaction factor analysis of data indicated antagonistic genotoxicity and oxidative damage of the NPs mixture.**
- **These results suggest cytogenotoxic effects of Ag NPs, CuO NPs and their mixture via oxidative stress in *Clarias gariepinus***

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Table: 2: Frequencies of micronuclei induced in peripheral erythrocytes of juvenile *C. gariepinus* exposed to Ag, CuO, Ag + CuO, and TiO_2 NPs for 28 days.

Conc. (mg/L)	MN Frequency per 1000 erythrocyte (Mean ± SE)				
	AgNPs	CuONPs	Mixture (Ag + CuO NPs)	TiO_2	IF ± SE_{IF} of Ag + CuONPs
NC	4.07± 0.55	4.07± 0.55	4.07± 0.55	4.07± 0.55	
6.25	4.40± 0.34	5.50± 0.44	6.47± 0.54	2.53 ± 0.73	0.63± 0.78
12.5	5.27± 0.16	7.27± 0.64*	8.27± 0.71***	5.53 ± 0.38*	-0.2± 0.97
25.00	6.33± 0.21*	8.80± 0.90***	10.67± 0.65***	8.27 ± 0.28*	-0.40± 1.13
50.00	7.73± 0.86***	7.20± 0.50*	10.20± 0.68***	12.06 ± 6.72*	-0.67± 1.20
100.00	7.00± 0.11**	8.58±1.16**	7.83± 0.32***	10.20 ± 0.38*	- 3.68 ± 1.20
PC	13.00 ± 0.99***	13.00 ± 0.99***	13.00 ± 0.99***	13.00 ± 0.99***	

NC: Negative control (Dechlorinated tap water), PC: Positive control 0.05mL/L Benzene. Significantly different from the control group at *p <0.05, **p < 0.01 and ***p < 0.001. A negative IF value denotes antagonism and a positive IF value denotes synergism.

Table 3: **Frequencies of nuclear abnormalities induced in peripheral erythrocytes of juvenile *C. gariepinus* exposed to Ag, CuO and Ag +CuO NPs for 28 days**

Conc. (mg/L)	Total nuclear abnormalities (TNA) per 1000 erythrocytes (Mean ± SE)		
	Ag NPs	CuO NPs	Ag + CuO NPs
NC	0.00± 0.00	0.00 ± 0.00	0.00 ± 0.00
6.25	0.53± 0.53	0.07 ± 0.00	3.47 ± 1.42
12.50	1.67 ± 1.29	2.20 ± 0.90	4.20 ± 0.71
25.0 0	0.00 ± 0.00	0.13 ± 0.13	0.00 ± 0.00
50.00	0.00 ± 0.00	3.53 ± 0.58	1.13 ± 1.13
100.00	0.00 ± 0.00	4.08 ± 2.22	0.00 ± 0.00
Benzene (0.5 mL/L)	6.00 ± 3.38*	6.00 ± 3.38*	6.00 ± 3.38*

NC= Negative control (Dechlorinated tap water). Significantly different from the control group (NC) at *p <0.05

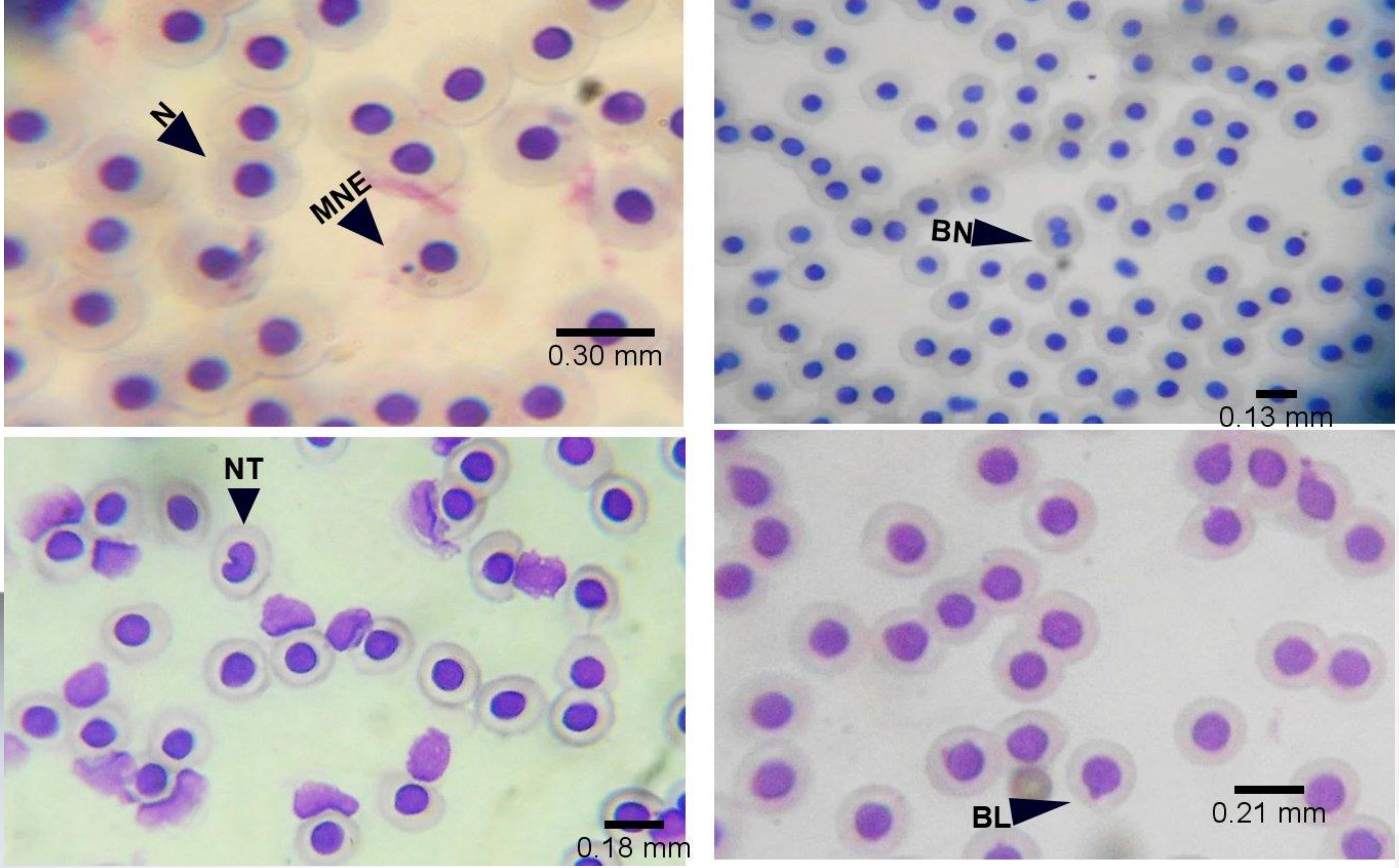

Fig. 11: Normal erythrocyte (N), micronucleated erythrocytes (MNE), binucleated cells (BN), notched (NT) and blebbed nuclei (BL) in peripheral blood of C. gariepinus exposed to AgNPs, CuONPs and their mixtures. (Mag.: X 1000)

Table 4: Oxidative stress parameters in the liver of *C. gariepinus* exposed to Ag, CuO NPs and Ag + CuO NPs

	SOD (unit/ mg protein)			CAT (mmole H_2O_2/min/mg protein)		
Conc. mg/kg	Ag NPs	CuO NPs	Ag + CuO NPs	Ag NPs	CuO NPs	Ag + CuO NPs
NC	0.17 ± 0.01	0.17 ± 0.01	0.17 ± 0.01	120.10 ± 43.74	120.10 ± 43.74	120.10 ± 43.74
6.25	0.09 ± 0.01	0.35 ± 0.03***	0.11 ± 0.07	39.67± 10.93*	41.11 ± 4.84**	88.00 ± 8.93
12.50	0.08 ± 0.03	0.19 ± 0.04	0.08 ± 0.02*	119.20 ± 4.10	12.06 ± 2.21***	80.42 ± 11.39
25.00	0.37 ± 0.08***	0.18 ± 0.02	0.07 ± 0.03**	141.00 ± 29.4	17.25 ± 0.00***	53.13 ± 0.00
50.00	0.30 ± 0.04**	0.27 ± 0.02**	0.13 ± 0.04	80.28 ± 0.60	3.908 ± 2.22***	50.77 ± 6.42*
100.00	0.15 ± 0.03	0.25 ±0.05*	0.08 ± 0.02*	87.06 ±18.09	3.137 ± 2.56***	85.01 ± 20.95
	GSH (nmol/mg protein)			MDA (nmol/mg protein)		
NC	774.30 ± 150.40	774.30 ± 150.40	774.30 ± 150.40	15.91 ± 2.50	15.91 ± 2.50	15.91 ± 2.50
6.25	240.70 ±. 26.05*	1257 ± 136.30**	629.5 ± 77.83	7.276 ± 2.39	20.12 ± 2.70	13.39 ± 2.90
12.50	481.20 ± 144.60	1143 ± 130.40*	784.3 ± 178.3	28.35 ± 17.1	20.42 ± 3.18	13.83 ± 3.20
25.00	912.00 ± 224.40	845.6 ± 174.80	285.6 ± 79.84*	18.22 ± 1.97	37.86 ± 2.5***	5.68 ± 0.18*
50.00	1127.00 ±166.70	840 ± 224.30	622.6 ± 162.40	24.26 ± 2.37	16.23 ±2.20	14.85 ± 3.97
100.00	778.30 ± 141.40	1244 ± 63.10**	696.9 ± 240.70	15.65 ± 1.79	29.06 ± 1.25***	7.326 ± 1.65*

NC= Negative control (Dechlorinated tap water). Data represents mean ± SE. * $p < 0.05$, ** $p < 0.01$ and *** $p < 0.001$ compared with

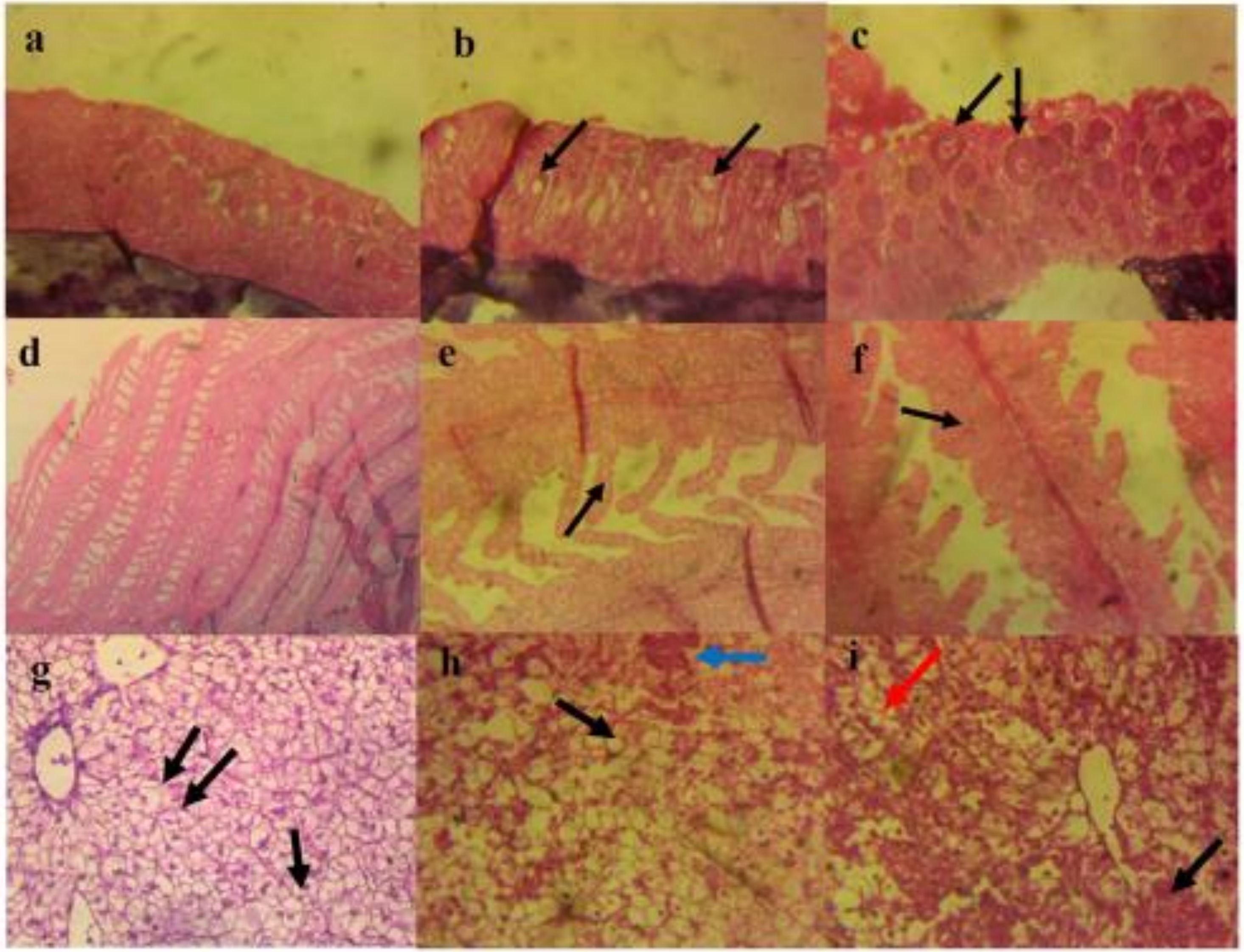

Fig.12: Sections showing histological changes in the skin layer, gill and liver of juvenile C. gariepinus exposed to Ag NPs, CuO NPs, 1:1 mixture for 28 days and controls. a Control: no visible lesion; b moderate hyperplasia of keratinocytes and goblet cells (arrows); c marked hyperplasia of alarm cells (arrow); d numerous and long filaments; the primary and secondary gill lamellae are normal in negative control group; e moderate hyperplasia of the lamellae (arrow); f moderate hyperplasia of the lamellae (arrow) and marked sloughing off of the secondary gill lamellae; g negative control: the hepatic plates are closely packed with the hepatocytes having large clear cytoplasmic appearance with the nucleus centrally placed; h centrilobular vacuolar degeneration (black arrow) of hepatocytes and atrophy of adjacent hepatocytes (blue arrow); i diffuse vacuolar degeneration

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ELSEVIER

Evaluation of cytogenotoxicity and oxidative stress parameters in male Swiss mice co-exposed to titanium dioxide and zinc oxide nanoparticles

Check for updates

Opeoluwa Fadoju[a], Olusegun Ogunsuyi[a], Olubukola Akanni[b], Okunola Alabi[c], Chibuisi Alimba[a], Oluwatosin Adaramoye[b], Sebastien Cambier[d], Santhana Eswara[e], Arno C. Gutleb[d], Adekunle Bakare[a,*]

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ORIGINAL ARTICLE

ANDROLOGIA WILEY

Alteration of sperm parameters and reproductive hormones in Swiss mice via oxidative stress after co-exposure to titanium dioxide and zinc oxide nanoparticles

Opeoluwa M. Ogunsuyi[1] | Olusegun I. Ogunsuyi[2] | Olubukola Akanni[3] | Okunola A. Alabi[4] | Chibuisi G. Alimba[1] | Oluwatosin A. Adaramoye[3] | Sebastien Cambier[5] | Santhana Eswara[6] | Arno C. Gutleb[5] | Adekunle A. Bakare[1]

Drug and Chemical Toxicology

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Taylor & Francis

Physiological and histopathological alterations in male Swiss mice after exposure to titanium dioxide (anatase) and zinc oxide nanoparticles and their binary mixture

Opeoluwa Ogunsuyi, Olusegun Ogunsuyi, Olubukola Akanni, Okunola Alabi, Chibuisi Alimba, Oluwatosin Adaramoye, Sebastien Cambier, Santhana Eswara, Arno C. Gutleb & Adekunle Bakare

Nucleus
https://doi.org/10.1007/s13237-020-00308-1

ORIGINAL ARTICLE

Check for updates

Interaction of titanium dioxide and zinc oxide nanoparticles induced cytogenotoxicity in *Allium cepa*

Opeoluwa M. Fadoju[1] · Oluwatobi A. Osinowo[1] · Olusegun I. Ogunsuyi[1,2] · Ifeoluwa T. Oyeyemi[3] · Okunola A. Alabi[4] · Chibuisi G. Alimba[1,5] · Adekunle A. Bakare[1]

Received: 10 October 2019 / Accepted: 2 January 2020

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Article

Toxicology and Industrial Health

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SAGE

Titanium dioxide nanoparticles-induced cytogenotoxicity and alterations in haematological indices of *Clarias gariepinus* (Burchell, 1822)

Opeoluwa M Ogunsuyi[1], Elizabeth O Adegoye[1], Olusegun I Ogunsuyi[2], Okunola A Alabi[3], Chibuisi G Alimba[1] and Adekunle A Bakare[1]

Lessons/ Implications

- **All the NPs and their mixtures induced cytogenotoxicity through mitodepression and chromosomal aberrations in the *Allium cepa* root cells.**

- **This is an indication that these NPs can alter cell cycle regulation and proliferate cells with damaged DNA resulting in cancer formation.**

- **The individual NPs and their mixtures induced clastogenicity and aneugenicity through micronuclei formation in the peripheral blood of *Clarias gariepinus* and bone marrow cells of *Mus musculus*.**

- **This may be due to the direct interaction of the NPs with the DNA and or indirect interaction of the NPs with the components of the mitotic spindles in the bone marrow cells.**

- **The individual NPs and their mixtures induced mutagenicity in the germ cells through increased frequency of abnormal sperm cells.**

- **TiO_2, ZnO NPs and their mixture altered the testicular architecture and reproductive hormones making them possible endocrine disrupting chemicals.**

- **These may lead to testicular/prostate cancer, reduction in fertility, embryonic/perinatal death, congenital malformations and reduction in pregnancy rate.**

- **Alterations in the clinical biochemical and antioxidants parameters suggest that the production of intracellular ROS was responsible for DNA damage in the somatic and germ cells of the eukaryotic organisms.**

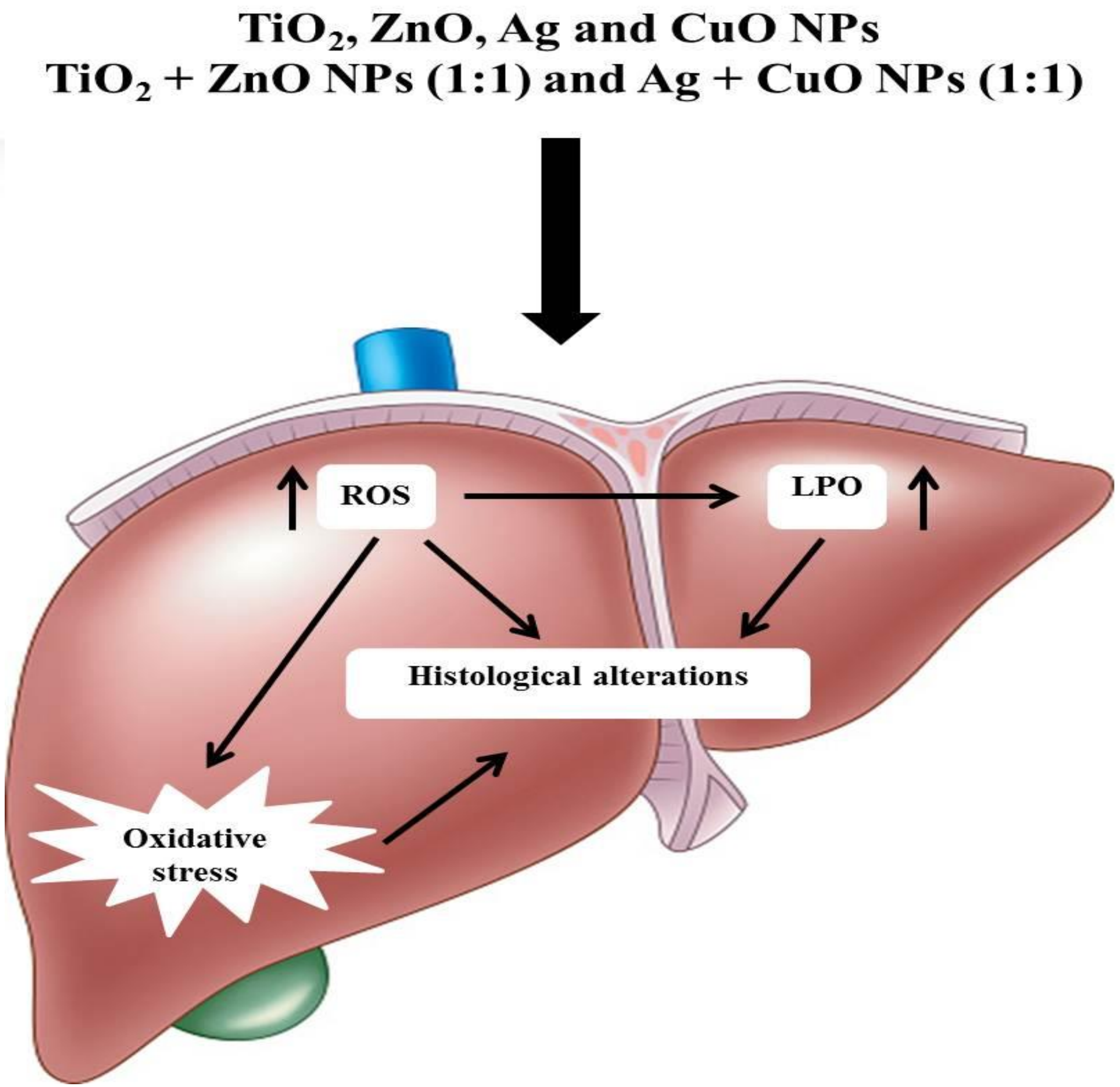

Fig. 13: Possible pathway of DNA damage induced by TiO_2, ZnO, Ag, CuO NPs, TiO_2 + ZnO NPs and Ag + CuO NPs.

RECOMMENDATIONS

- **There should be ways to facilitate safer synthesis and minimise the release of these NPs from the factories to the environment, as they are persistent and nondegradable.**

- **These NPs should be prohibited for remediation due to the adverse effects they induce on humans and the environment.**

- **More epidemiological studies be carried out especially on reproductive toxicity to have a conclusive understanding on the health and safety of these NPs.**

- **Establishment of a public dialogue is essential to create awareness on the adverse effects, and also to regulate the disposal of TiO_2 and ZnO NPs in order to protect the environment.**

On going research/interests

- **Chromosomal damage and recovery assessment in Allium cepa exposed to silver and copper oxide nanoparticles and their binary mixture (written MS)**
- **Antimicrobial activity and mitotic assessment of some medicinal plants**
- **Establishment of Alternative models to animal toxicity testing.**
- **Anticarcinogenic potentials of Nigerian medicinal plants.**
- **Genotoxicity assessment of xenobiotics in Nigerian environment**

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THANK YOU FOR LISTENING