

**chemoprevention of colonic aberrant crypt foci
by Schiff based zinc (II) complex in
azoxymethane-induced colorectal cancer in
rodents**

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□ **Background:** Based on the potential of Schiff base compounds to act as sources for the development of cancer chemotherapeutic agents, this in vivo study was performed to investigate the inhibitory properties of the synthetic Schiff base compound Zinc (II) on colonic aberrant crypt foci (ACF).

□ **Methodology:**

□ This study involved **five groups** of male rats. The **negative control group** was injected with normal saline once a week for 2 weeks and fed 10% Tween 20 for 8 weeks, the **cancer control group** was subcutaneously injected with **15 mg/kg azoxymethane** once per week for two consecutive weeks, the **positive control group** was injected with **15 mg/kg azoxymethane** once per week for two consecutive weeks **and 35 mg/kg 5-fluorouracil** (injected IP) for 4 weeks, and the **experimental groups** were first injected with 15 mg/kg azoxymethane once per week for two consecutive weeks and then fed **25 or 50 mg/kg** of the Schiff base compound once a day for 8 weeks

Application of the Schiff base compound **suppressed** total colonic **ACF** formation by up **to 72% to 74%** when compared with the cancer control group..

Histologically, all treatment groups exhibited **significant decreases** in dysplasia compared to the cancer control group.

Immunohistochemical staining demonstrated **down-regulation** of the PCNA protein. and up-regulation of Bax expression compared with the AOM control group.

□ **Conclusion:**

□ The current study demonstrated that the Schiff base zinc (II)) compound has promising chemoprotective activities that are evidenced by significant **decreases** in the numbers of **ACFs** in azoxymethane-induced colon cancer.

□ Colorectal Cancer (CRC)

∅

∅ Also known as colon cancer or bowel cancer

∅ **Third** commonest cause of cancer deaths in world

∅ About **3600 new cases** are diagnosed every year in USA, in both women

□

∅ Accounts for 13% of all cancers and is the **second** most common cancer death in the Western world



□ **Aberrant crypt foci (ACF)**

∅ The aberrant crypt foci (ACF), or specific

□ **dysplastic** subset of these lesions, are seen as an early precursor stage to **adenomas** and **colon cancer**

∅

∅ ACF itself is a **monoclonal** structure that

□ arises from **mutations** within a single crypt **stem cell**

□ Synthetic compound and defense against carcinogenesis

- § It is important to identify the synthetic active compounds
-
- § and the relationship of structure with the biological activity
-
- § and report the correct manner for using them with proper and efficient route of administration

□ Zinc is actual vital for mostly in all cellular purposes and crucial trace component with a diversity of biological characters in organisms. Zinc, as a catalytic constituent of more than 300 enzymes, particularly those included in the antioxidant protection system, for example metallothionines, zinc superoxide dismutase, is a trace component that entices a great deal of consideration in anti-carcinogenic actions (Chowdhury et al., 2020; Sun et al., 2021)

□ Schiff bases are cluster of compounds comprising an azomethine group (-C=N-), have drawn consideration for a long period due to their biological actions.

□

□ The synthetic Schiff base zinc (II) complex have active biological medieties and own various pharmacological actions as a potent antioxidant, gastroprotection, cancer chemotherapeutical mediator, antibacterial, antifungal, antioxidant, DNA binding, anticancer activities and anti-inflammatory activities.

□ The main objective of this study is to evaluate chemoprevention effects of Zinc (II) schiff based compounds against AOM-induced ACF in rats.

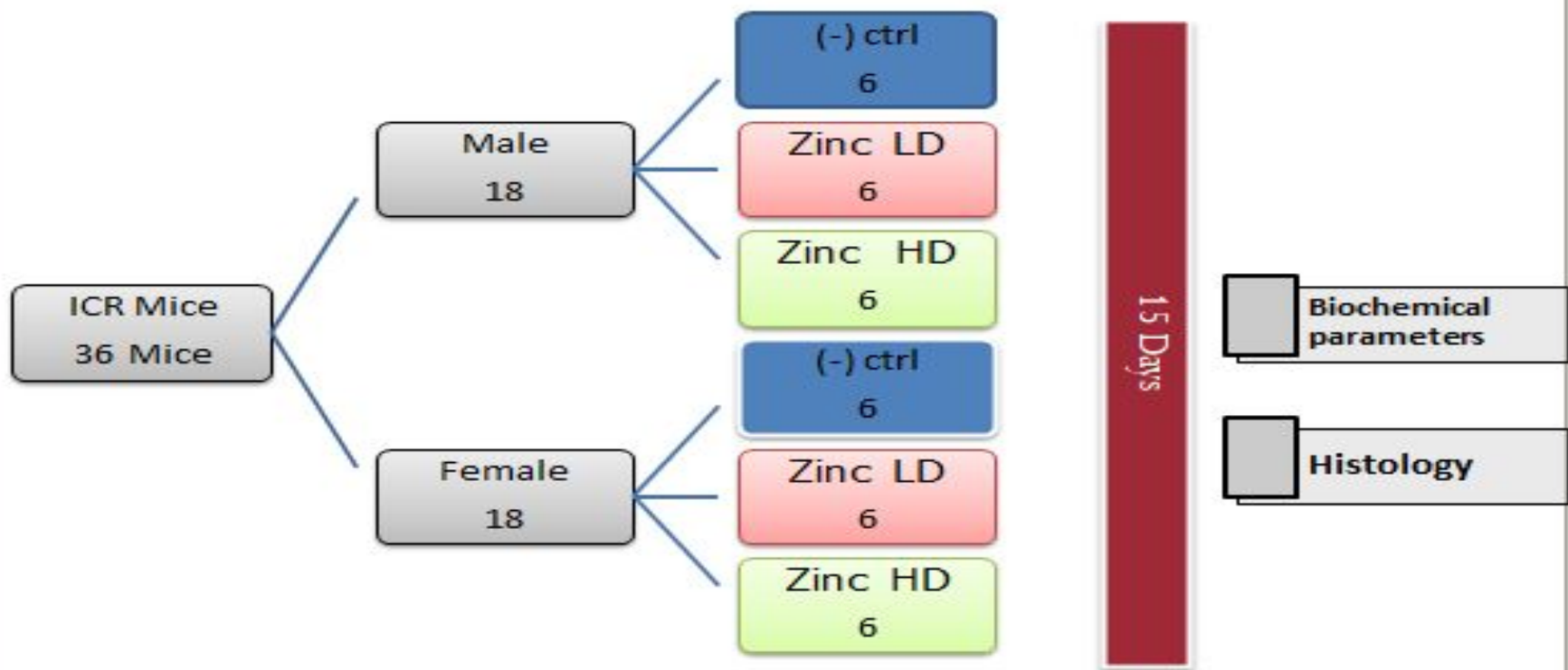
***In vivo* study**

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graph TD; A["In vivo study"] --- B["Acute toxicity test"]; A --- C["Induction and chemoprevention of colon cancer"]
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Acute toxicity test

Induction and chemoprevention of colon cancer

Research Methodology



**Azoxymethane
(AOM)**

Used to induce
colon cancer in rats
and mice.

Abnormalities in
Transforming
Growth Factor
beta (TGF- β)
signalling

C₂H₆N₂O

Is a potent
carcinogen

determine the
chemopreventative
effectiveness of
Commonly used to
particular foods

Colon cancer Experiment

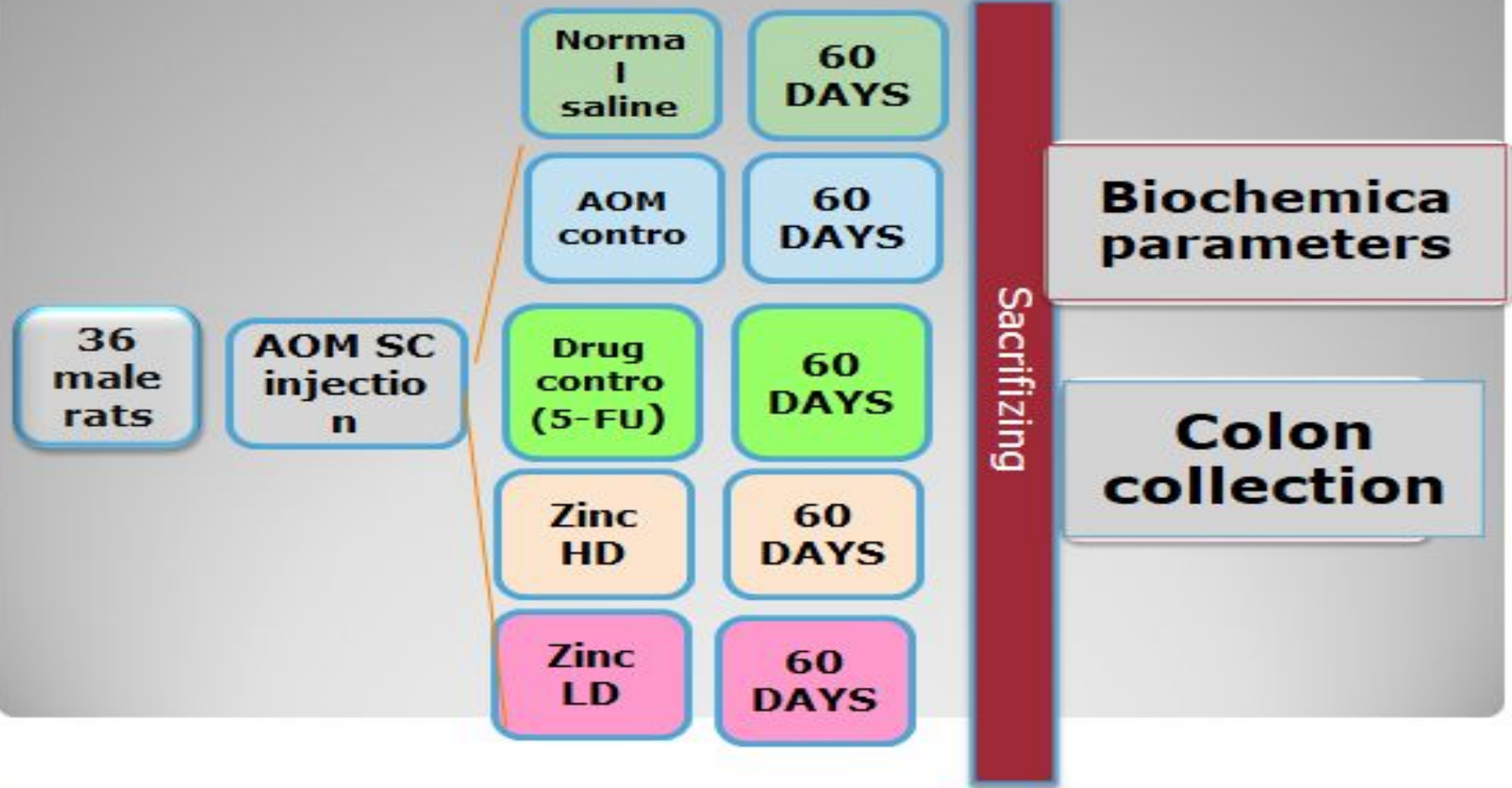
Azoxymethane (AOM) does not interact with DNA directly

*AOM is metabolised into methylazoxymethanol by (cytochrome P450) CYP2E1, causes DNA mutations

*Methylazoxymethanol then breaks down into formaldehyde and a highly reactive alkylating species, probably the methyldiazonium

*This chemical actually causes alkylation of DNA guanine to O6-MEG and to O4-methylthymine. These include K-ras, β -catenin and TGF β pathways.

*AOM has been shown to cause K-ras gene transversion mutation from G: C to A: T at codon 12



**Histological
examination**

**Gross
morphology**

**Colon
samples**

Immunohistochemistry



Results and Discussion

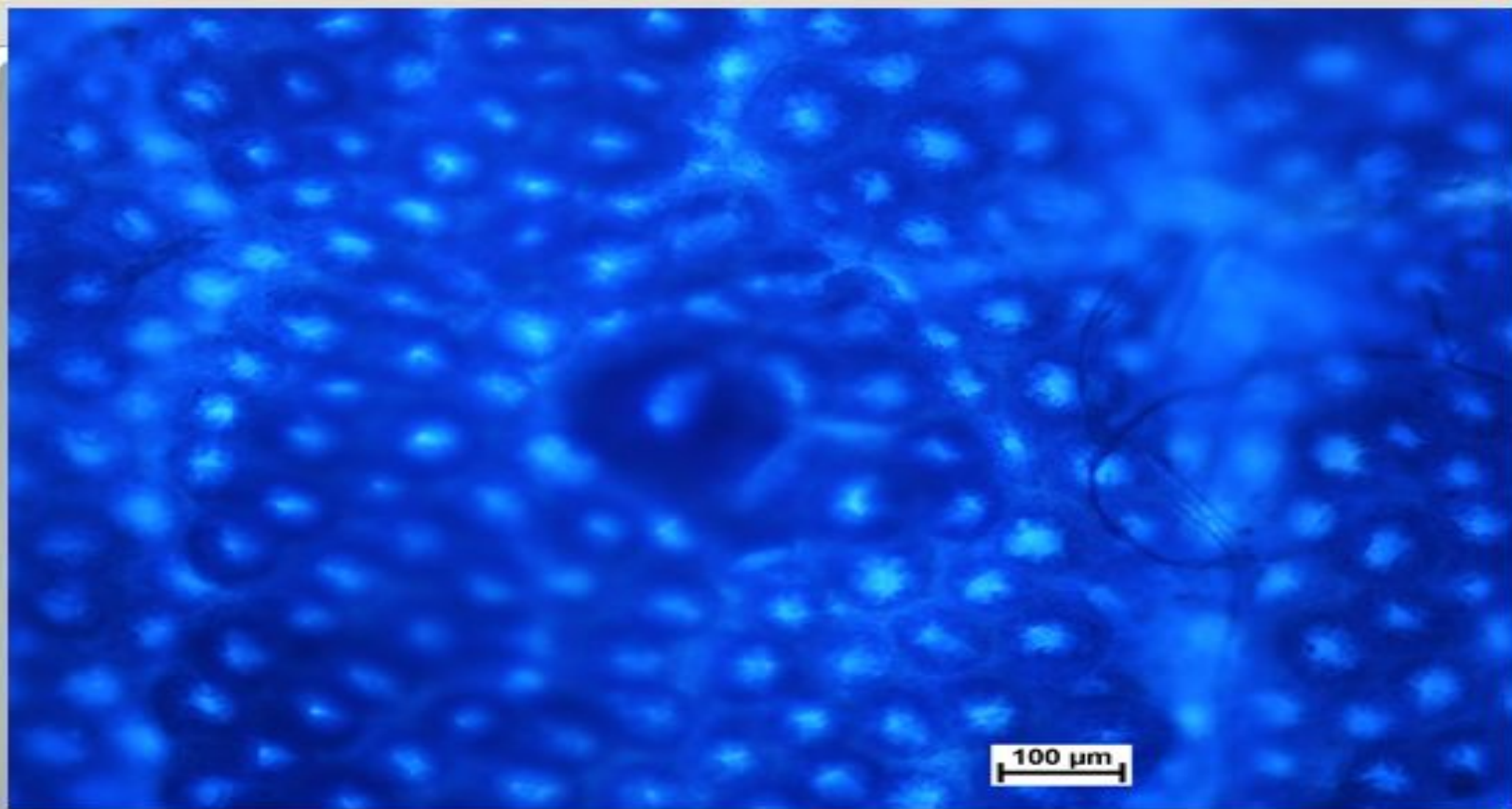




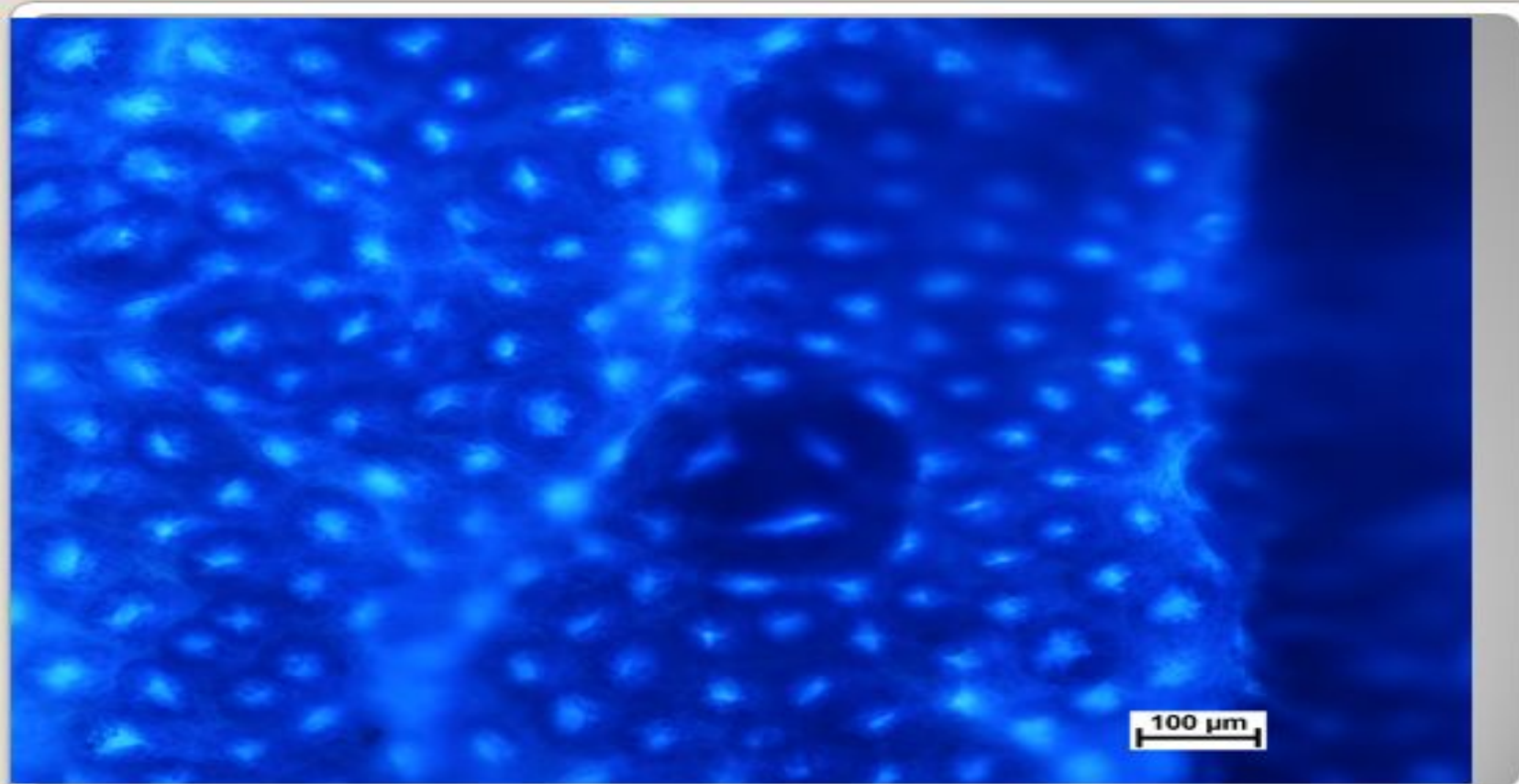
G1 10x Normal control (MB stain)



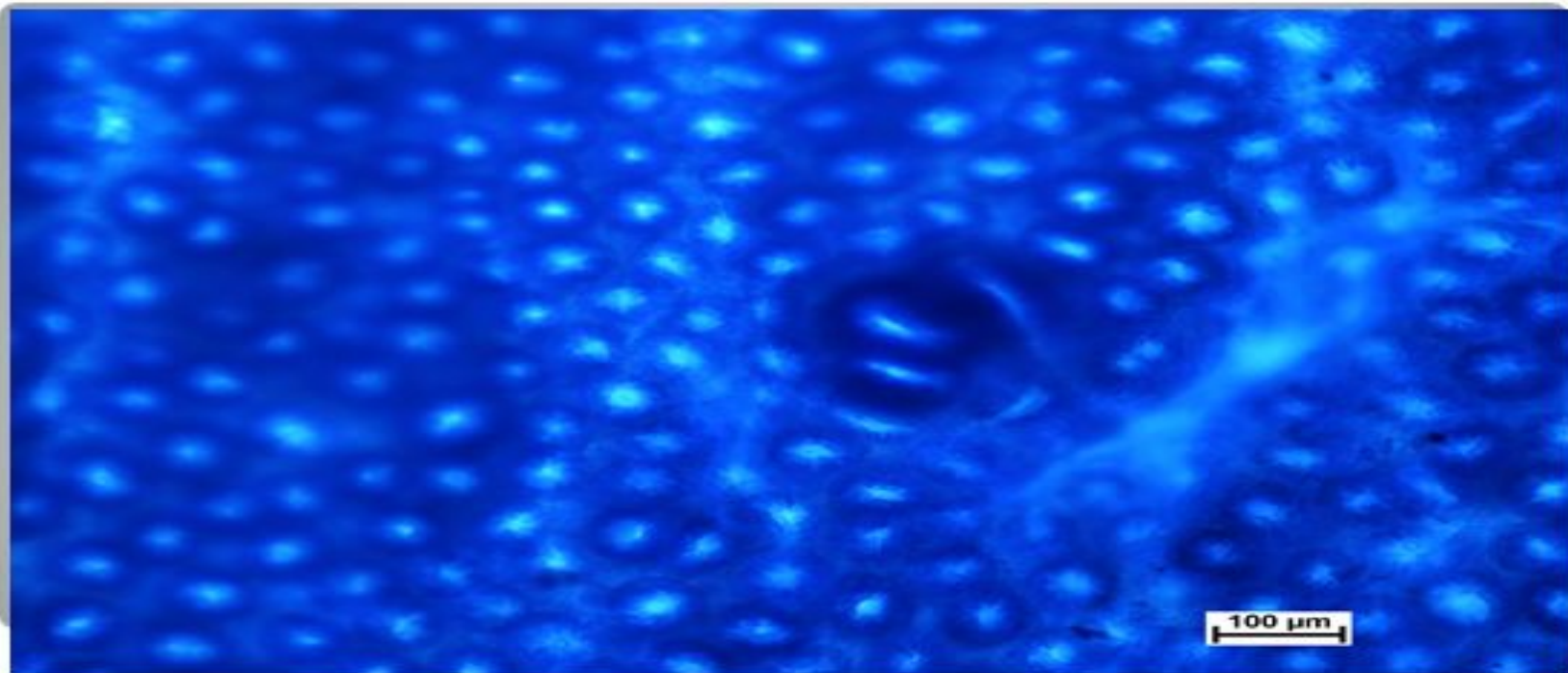
G2 10x AOM control (MB stain)



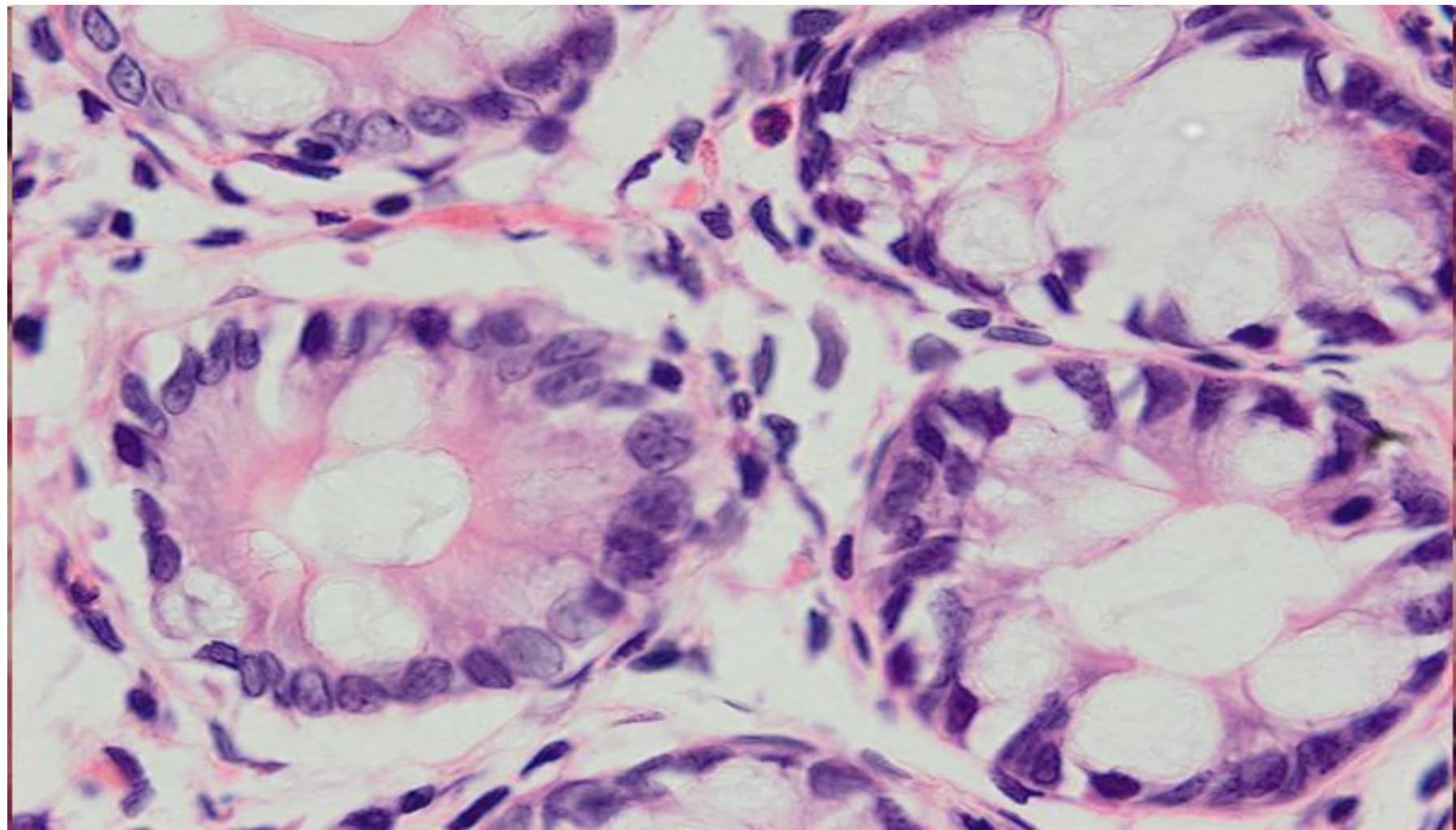
G3 10x 5-FU (Reference drug) MB stain

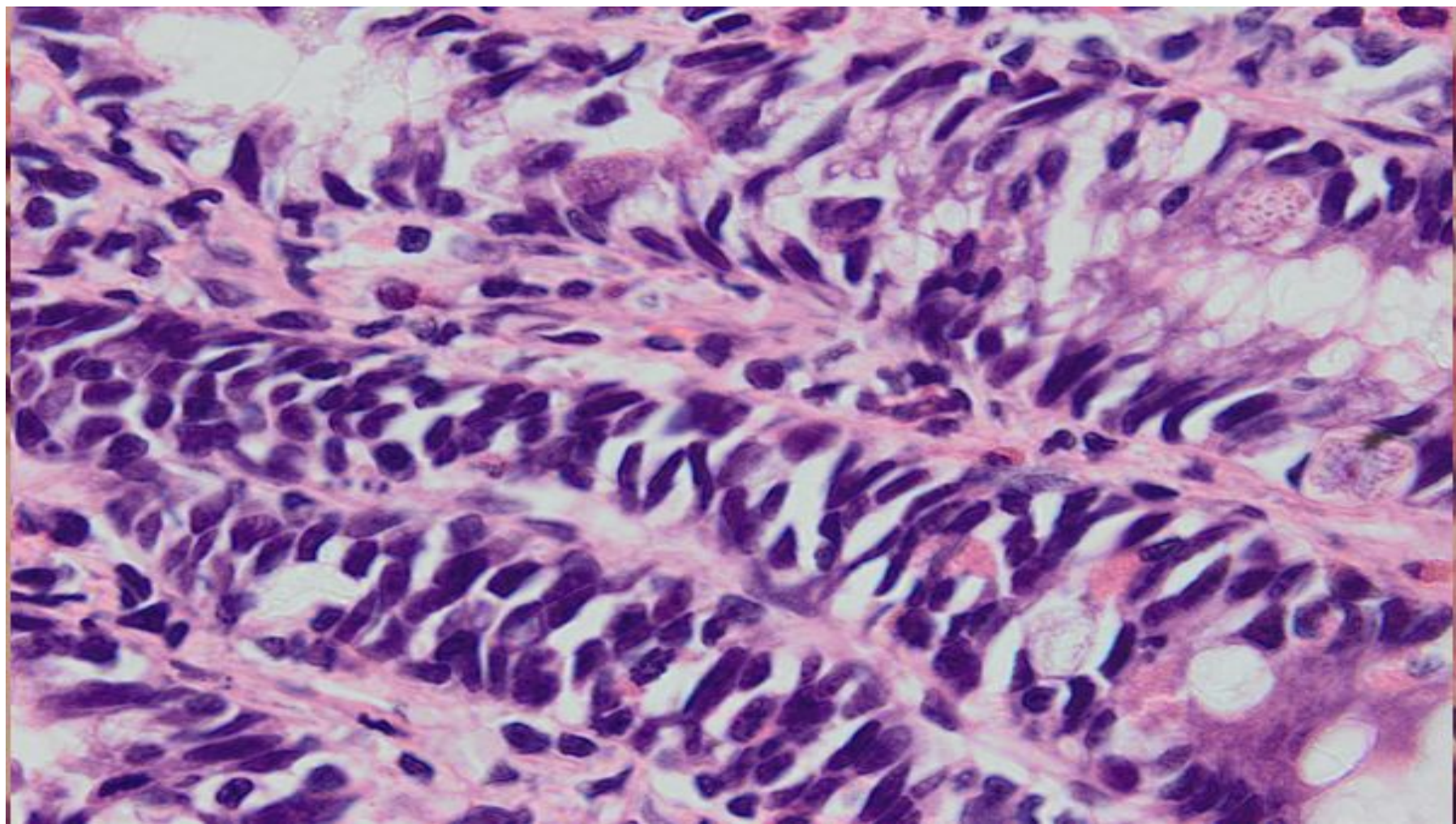


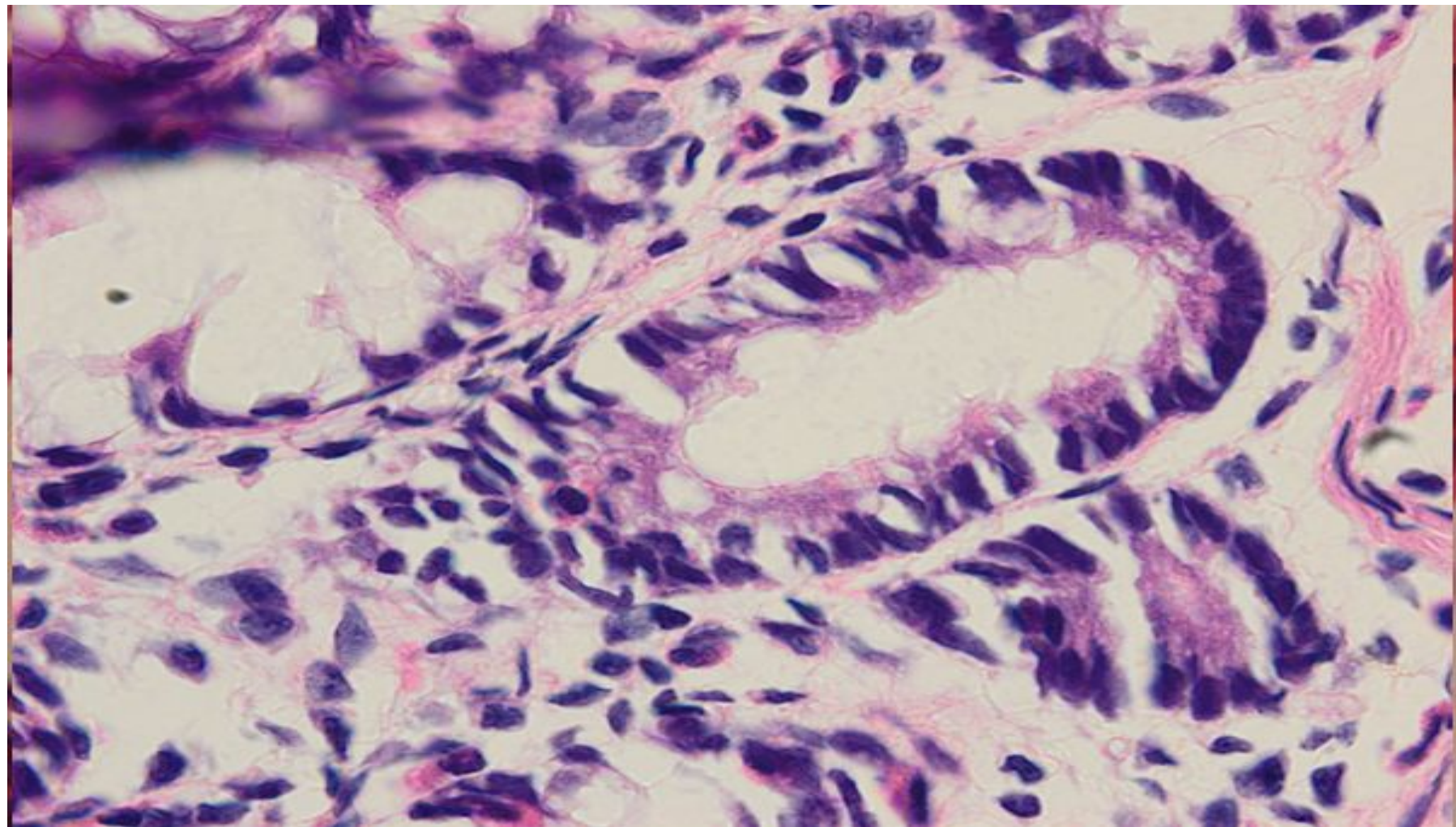
G4 10x 25 mg/kg Schiff bas zinc (MB stain)

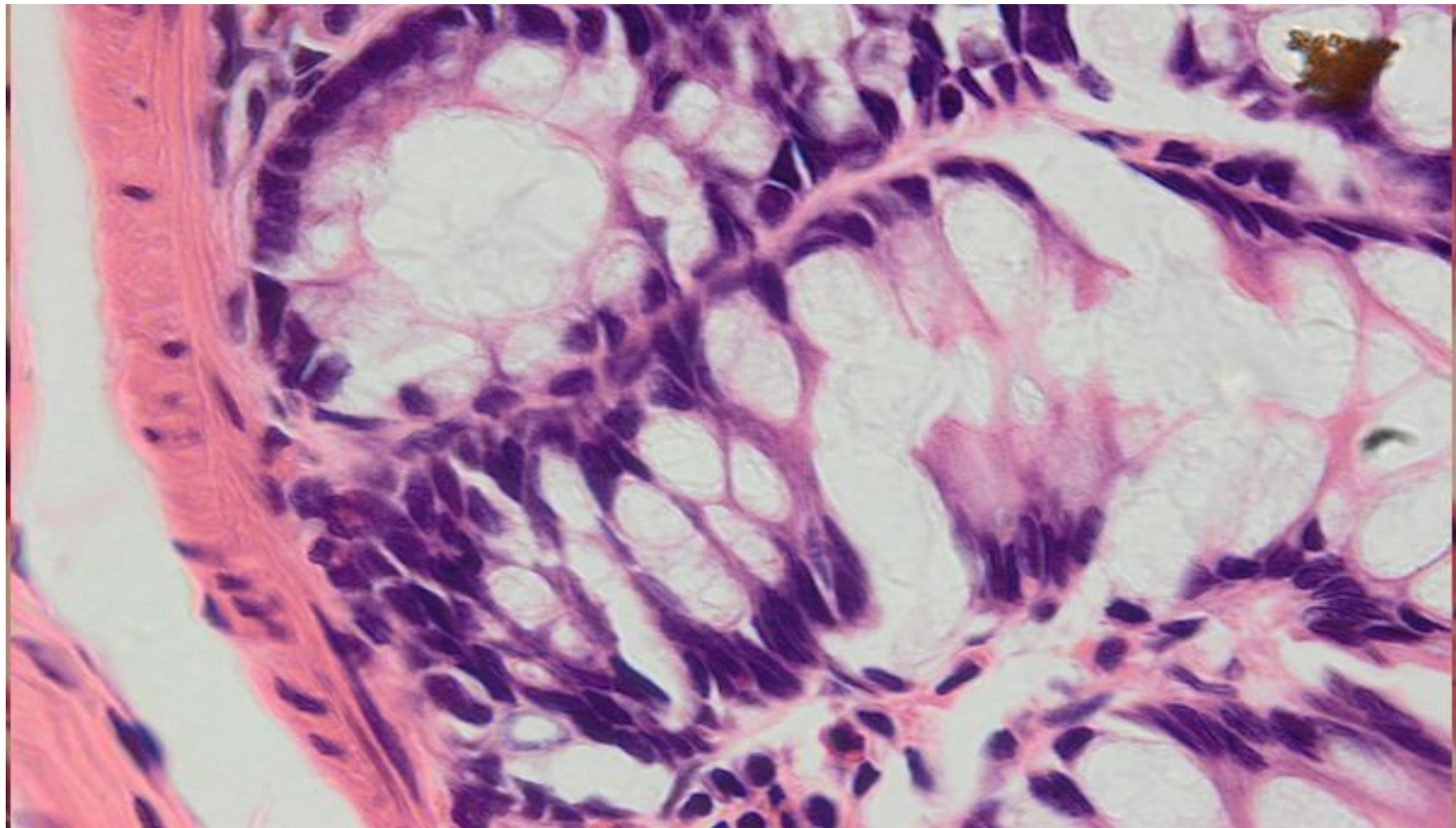


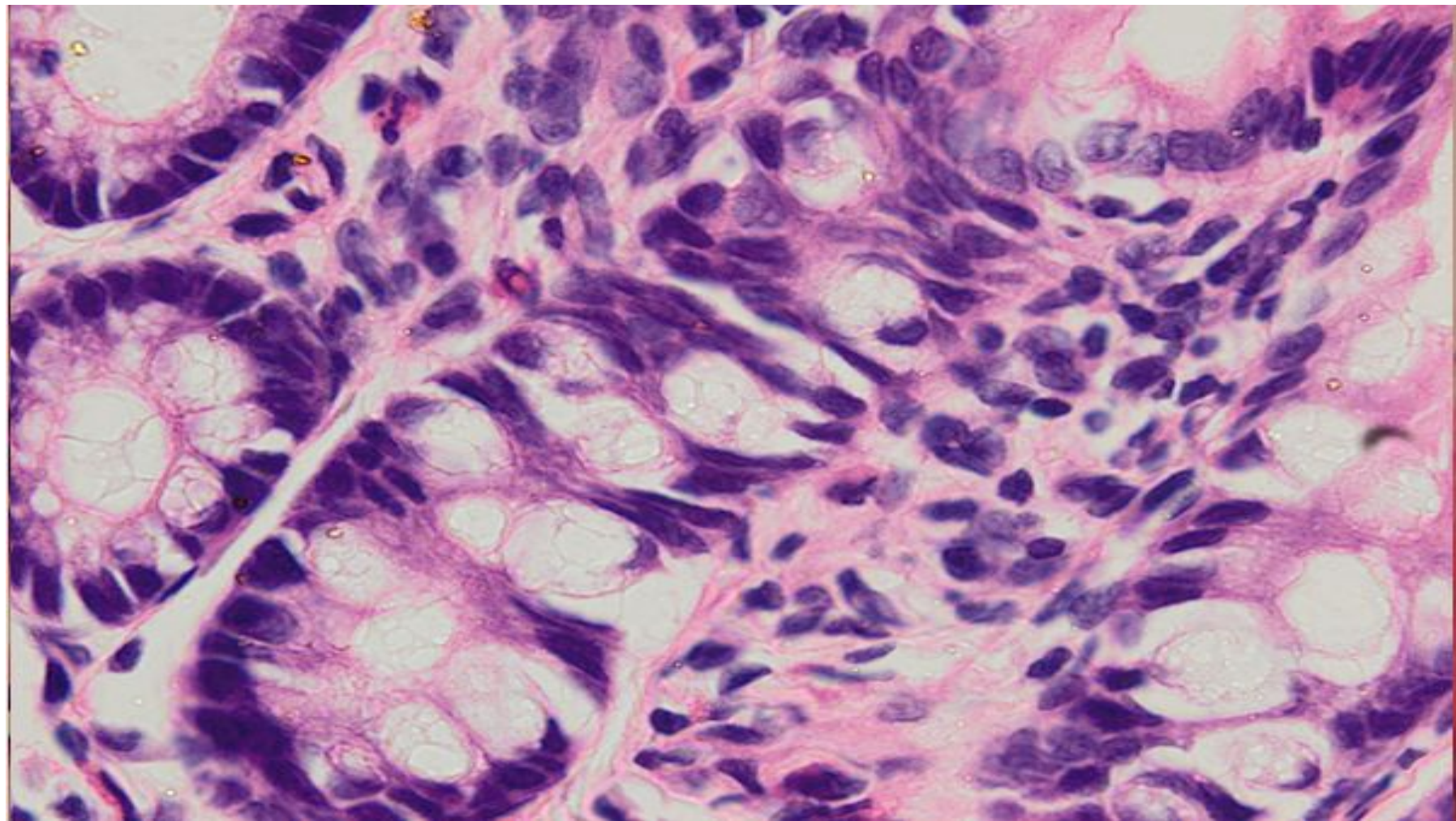
G5 10x 50mg/kg Schiff base zinc (MB stain)

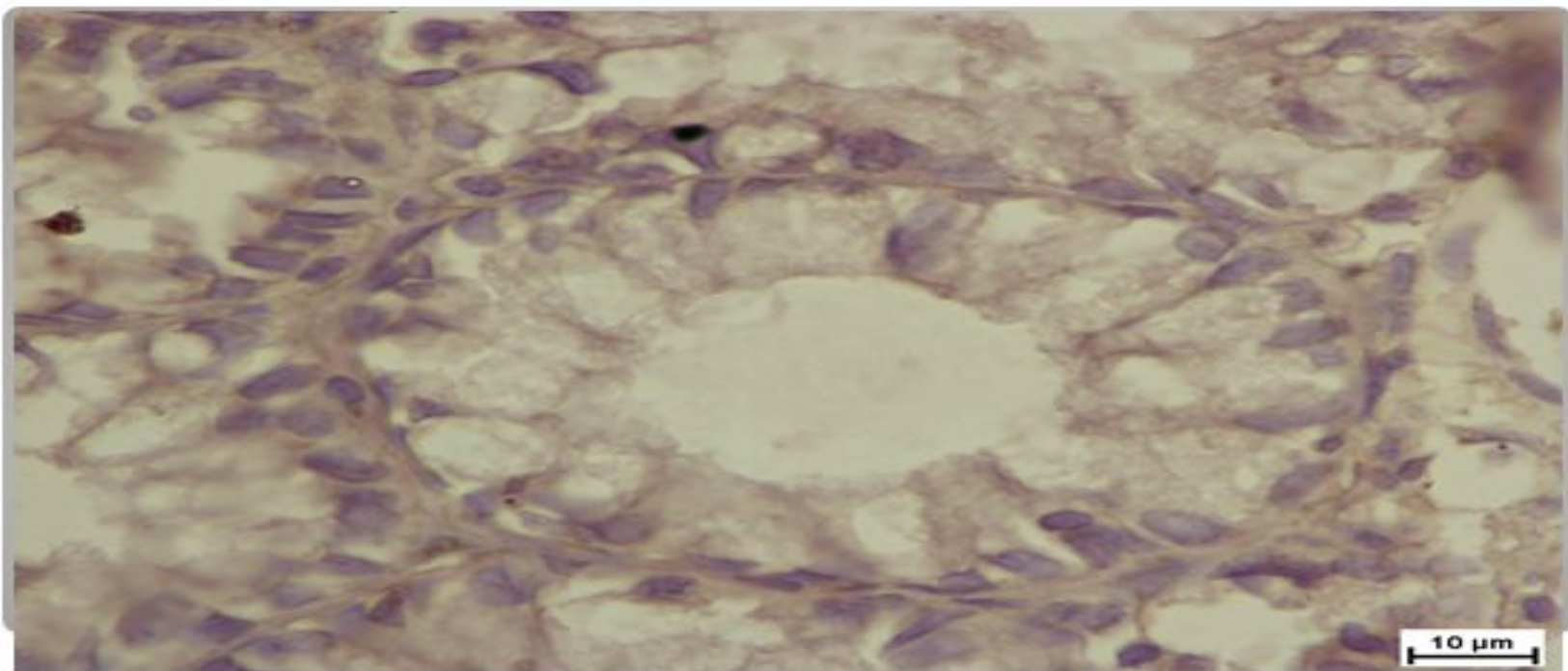




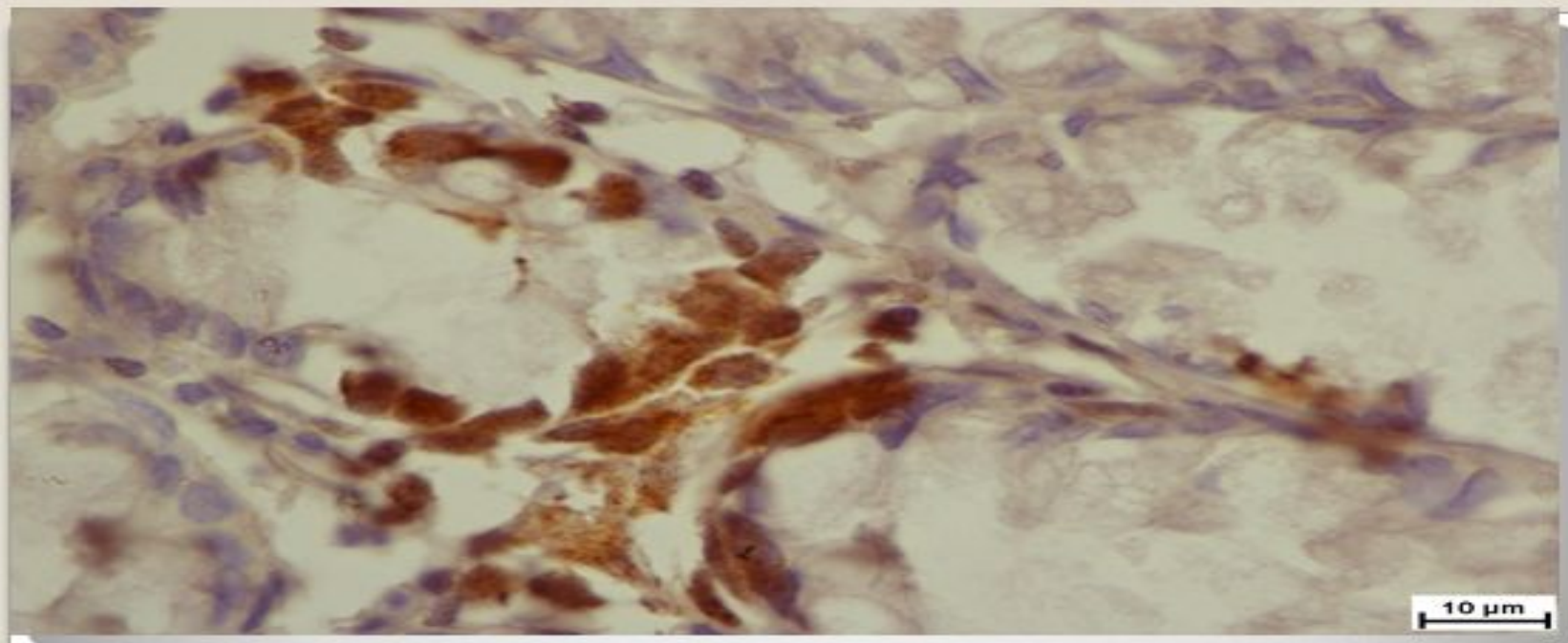




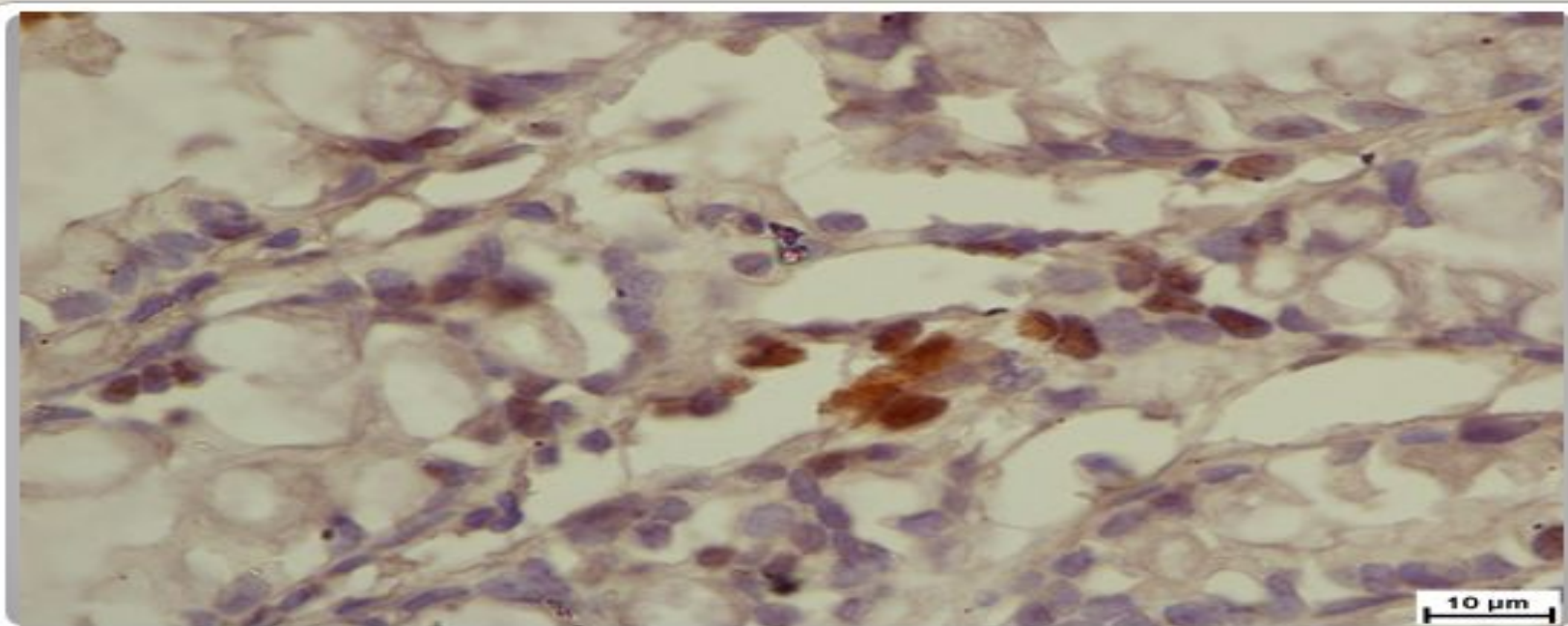




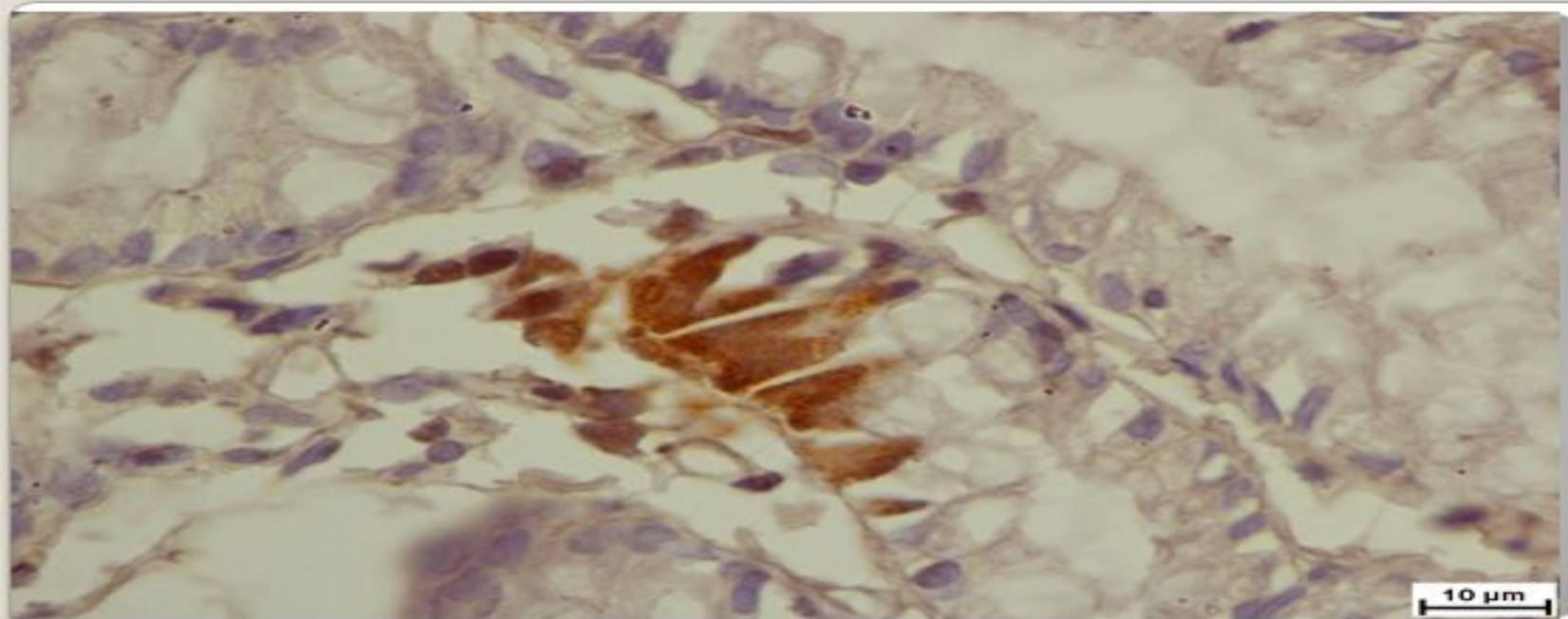
G1 100x Normal PCNA (IHC Stain)



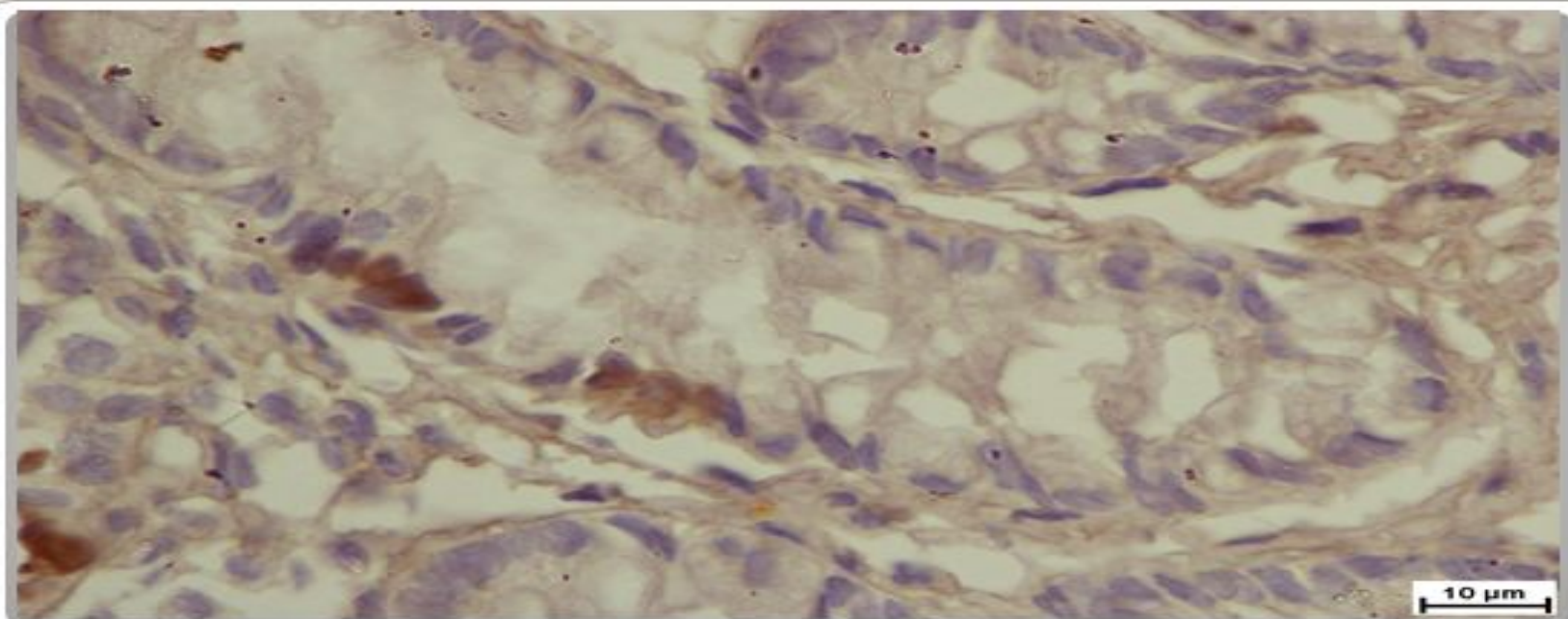
G2 100x AOM control PCNA (IHC stain)



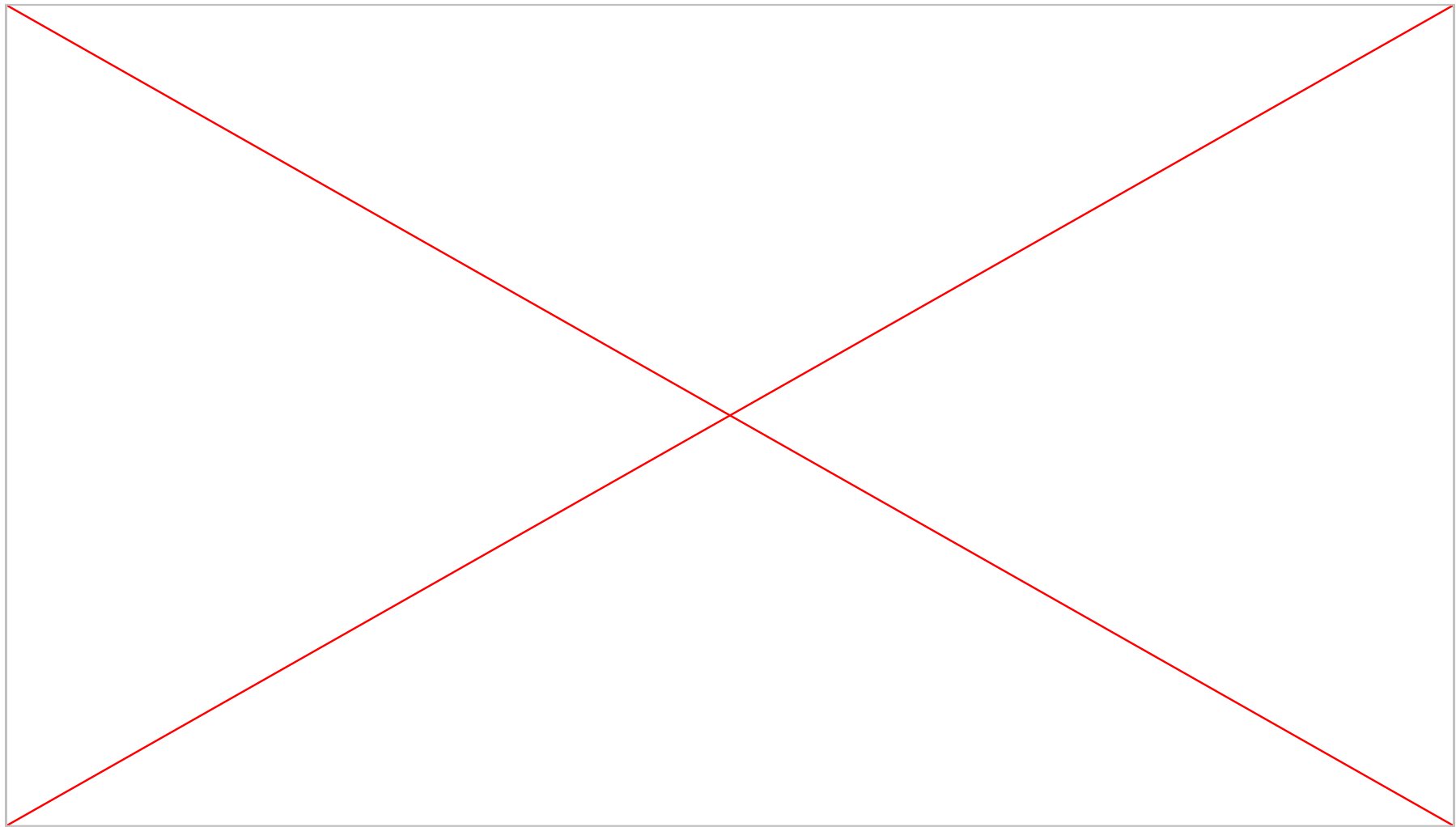
G3 100x 5-FU PCNA (IHC stain)

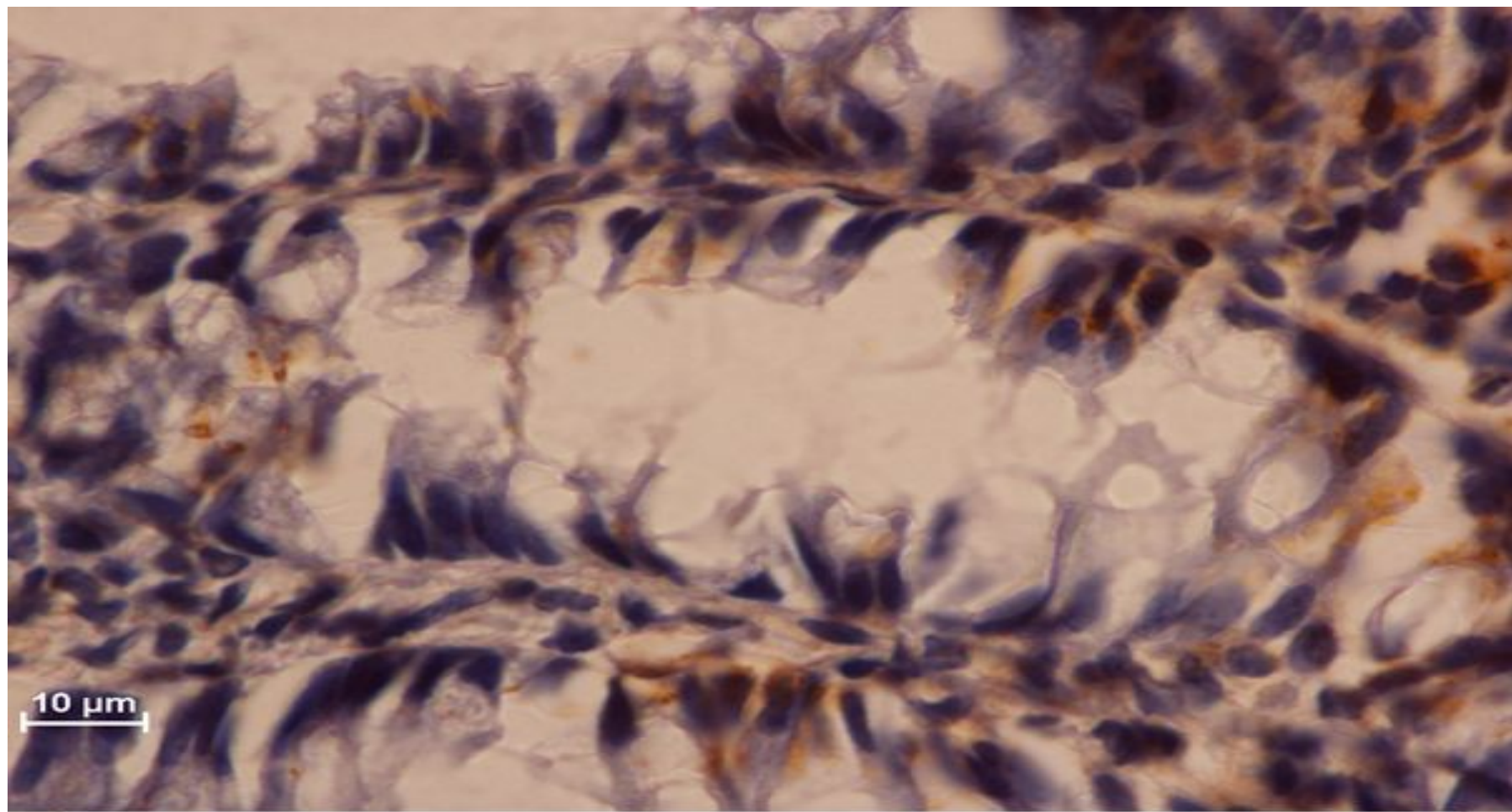


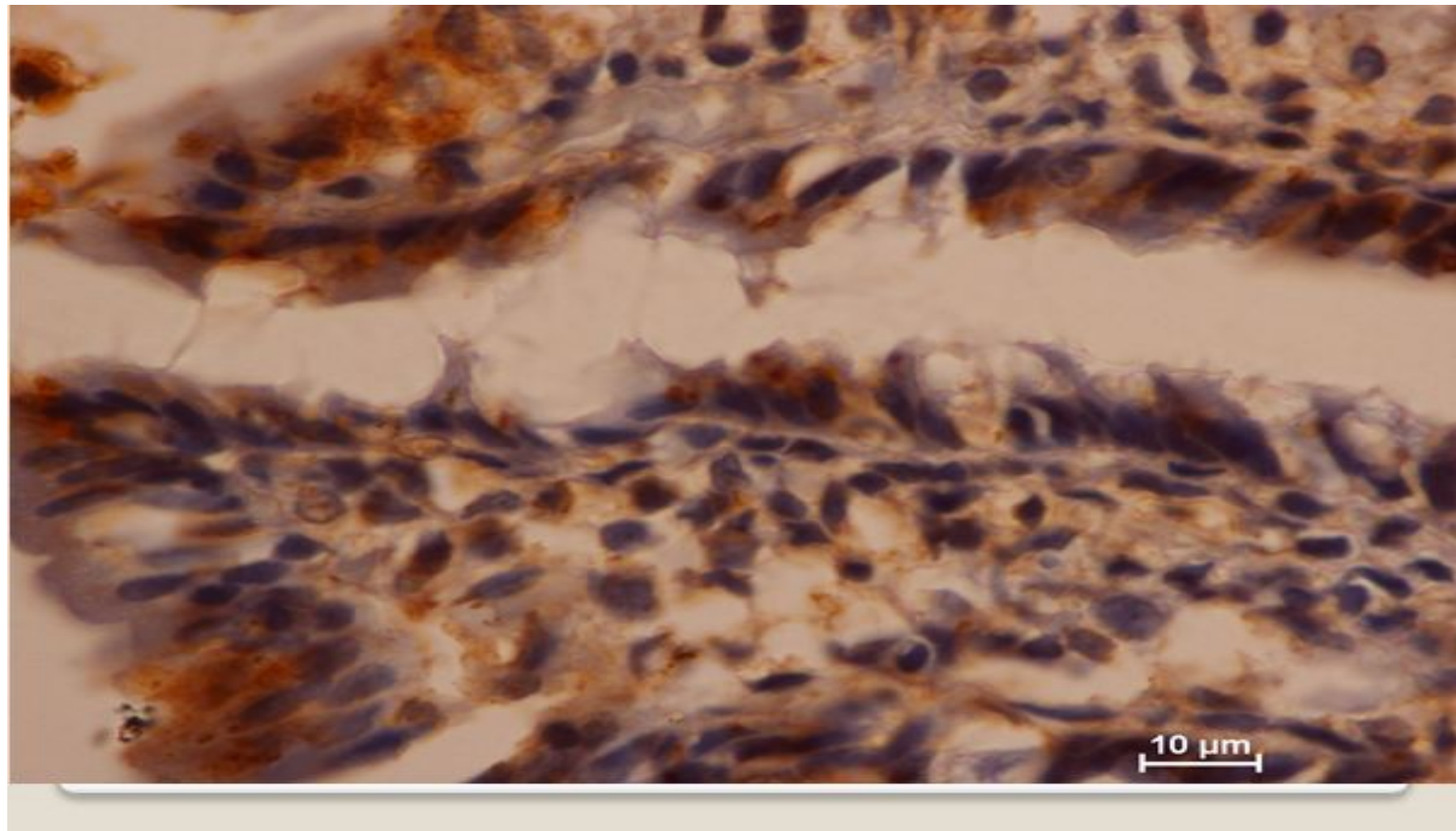
**G4 100x 25 mg/kg Schiff base zinc PCNA
(IHC Stain)**

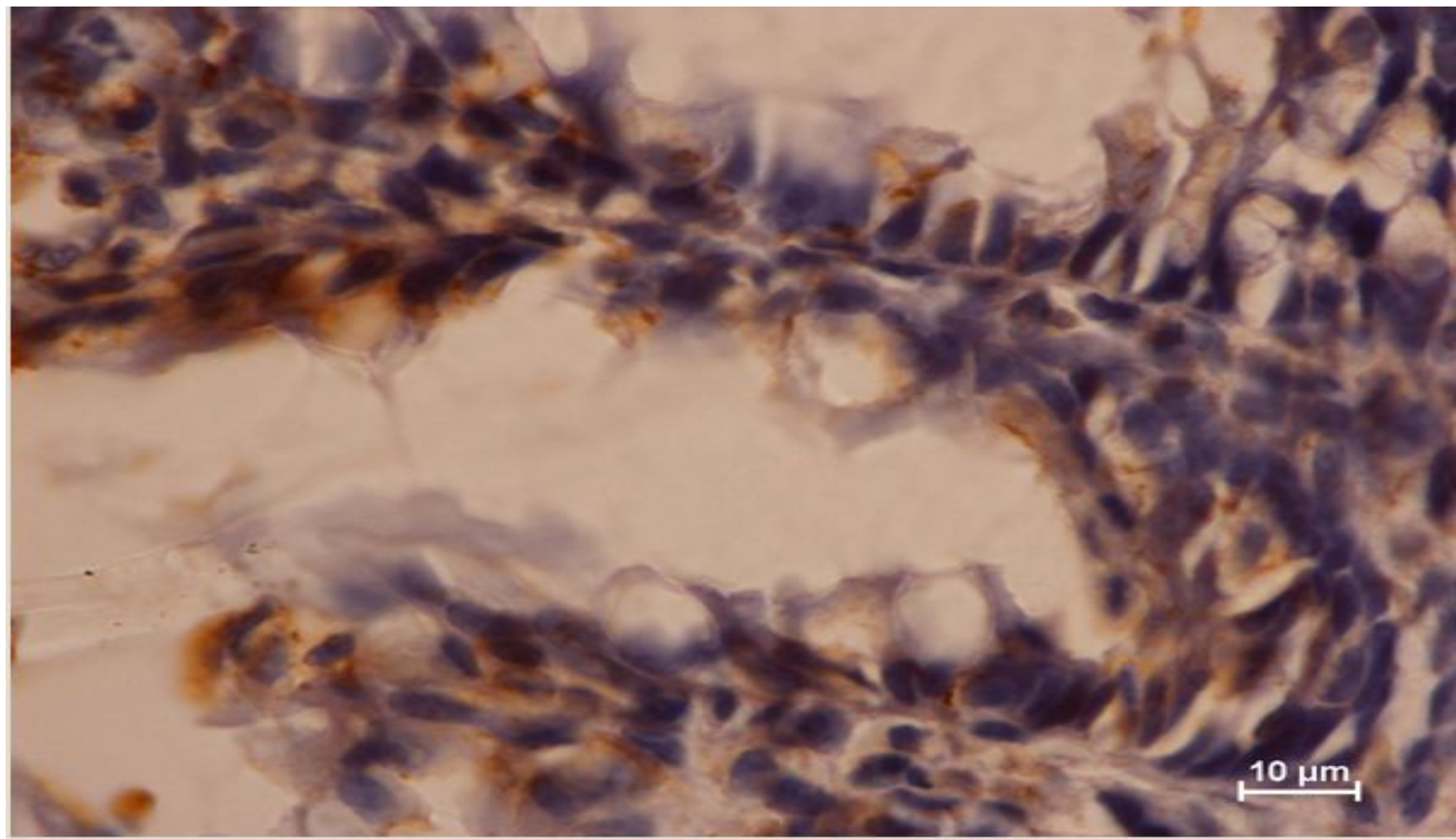


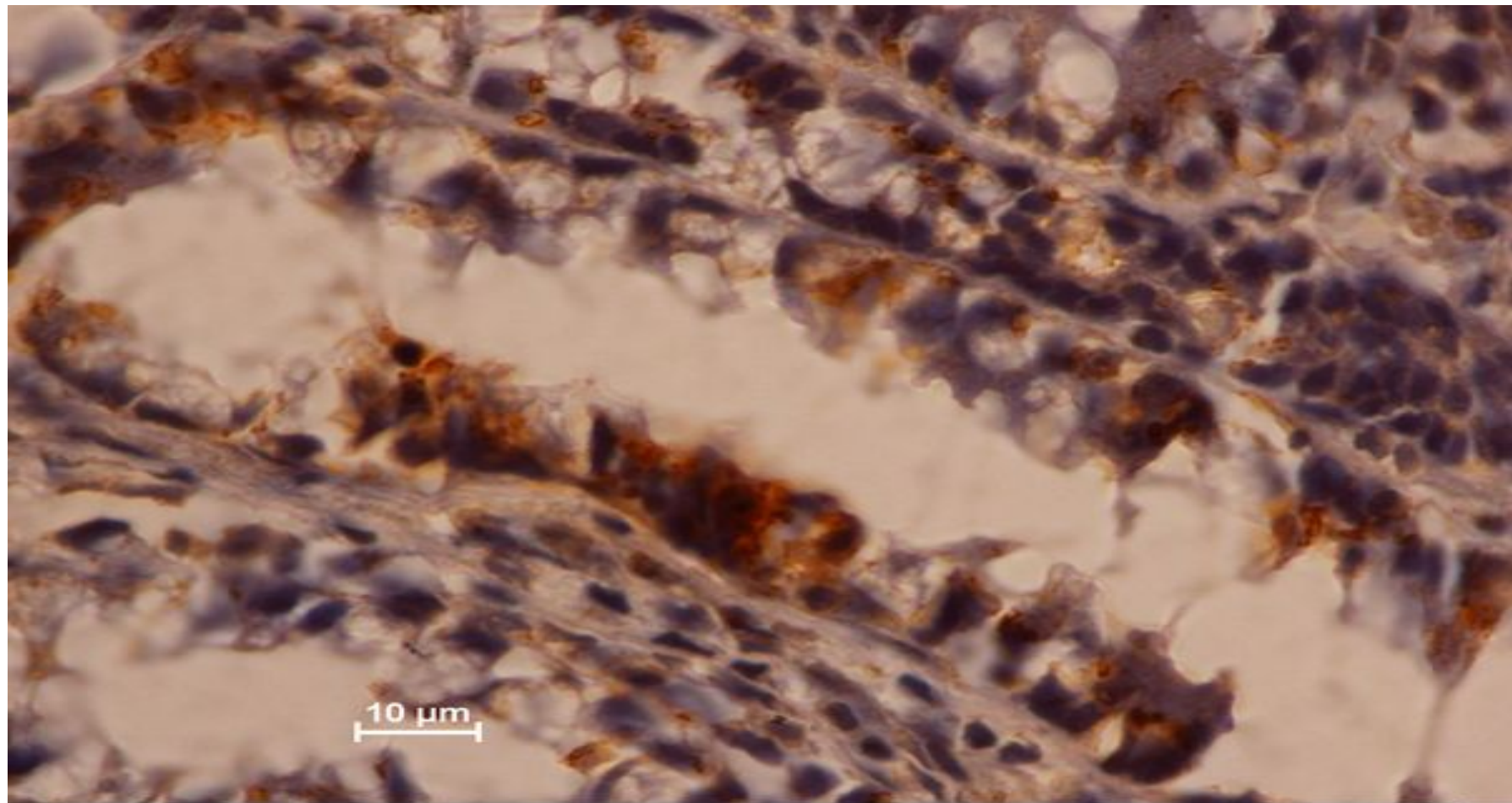
**G5 100x 50 mg/kg Schiff base
zinc PCNA (IHC Stain)**











Conclusion

Collectively, the results presented in this study revealed the promising **chemoprotective activity** of Zinc (II) complexes through the supporting evidence such as:

Significant **decrease** in number of **ACF**, , **down-regulation** of **PCNA** and **up-regulation** of Bax proteins expression.

*THANK YOU FOR
YOUR ATTENTION!*

