## بسم الله الرحمن الرحيم



## أهمية مشتقات الإبل في صحة الأنسان Uncovering Novel Compositions Derived from Camels and Health Benefits

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### **Outlines**

 Medicinal uses of camel milk, camel urine, and Combinations

 Products Inspired/Derived from Bioactive Compounds in Camel Urine/camel Milk

- What are the Evidences?
  - -Anti-Proliferative, Anti-Inflammatory, Anti-Angiogenesis, Anti-Thrombotic, Anti-sickling,...

Summary & Conclusions

### قال تعالى: (أفلا ينظرون إلى الإبل كيف حلقت) صورة الغاشية

"Do they not look at the camels, how they are created?"

عن أنس ان رهطاً من المدينة قدموا على النبي صلى الله عليه وسلم فقالوا: إنا اجتوينا المدينة فعظمت بطوننا وإرتهشت أعضادنا فأمرهم النبي صلى الله عليه وسلم أن يلحقوا براعي الإبل فيشربوا من ألبانها وأبوالها حتى صلحت بطونهم وألوانهم.

رواه البخاري



### Medicinal uses of camel milk & urine

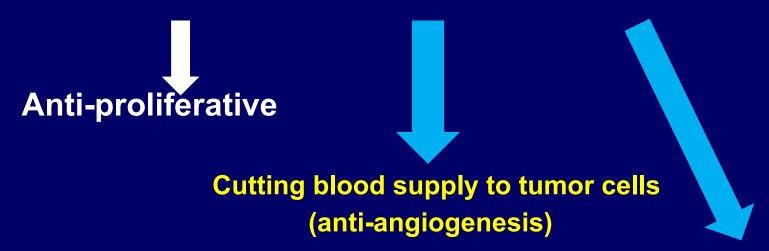
- Anti-cancer
- Antithrombotic without systemic anticoagulation

Pathological Angiogenesis (DR, AMD,..)

Anti-Sickling / Antiadhesive in Sickle Cell

### Medicinal uses of camel Urine/Milk – cont.

Drug actions against cancer



Immunotherapy/
Immune modulations

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## In vitro Anticancer Agent I-Tissue Culture Study of Human Lung Cancer Cells A549 II-Tissue Culture Study of Mice Leukemia Cells L1210

<sup>1</sup>F.A. Khorsid and <sup>2</sup>S.S. Mushref

healthy tissue and the function of the vital organs'. Tissue culture of human lung cancer cells and mice leukemia cells were compared with that of normal (human skin fibroblasts) in studying the effect of PM 701. This agent proved to induce apoptosis of the cancer cells without detrimental effect on normal cells; through its effect on the nuclei, limiting the division of cells, causing degeneration in apoptotic manner. PM 701 exhibited nourishing

### Faten A. Khorshid

Findings: 2009

 PMF (extract of PM 701: Sterile natural product) and its subfractions:



 Variable and notably high cytotoxic activity against the tested cell lines:

hepatocellular carcinoma (HEPG2),

colon carcinoma (HCT 116) and

human glioma (U251) cells.

**Lung cancer cells** 

Leukemic cells



#### Journal of Alternative and Complementary Medicine, 2010

### The anti-platelet activity of camel urine

Abdulqader Alhaidar1, Abdel Galil M Abdel Gader1, Shaker A. Mousa1,2

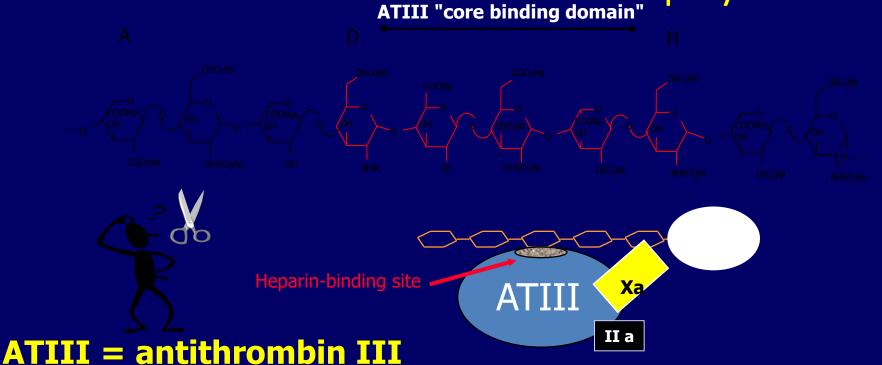
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Alhaidar A, Abdel Gader AG, Mousa SA. The antiplatelet activity of camel urine. *J. Altern Complement Med.* 2011 Sep;17(9):803-8.

# Heparin Depolymerization Processes in LMWH Preparations

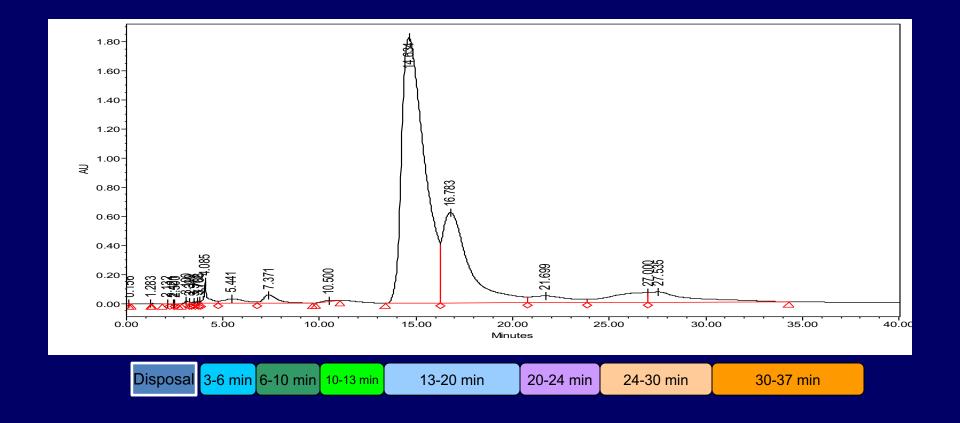
How is the endogenous heparin chain depolymerized?



Pentasaccharide is the smallest sequence that has affinity for ATIII

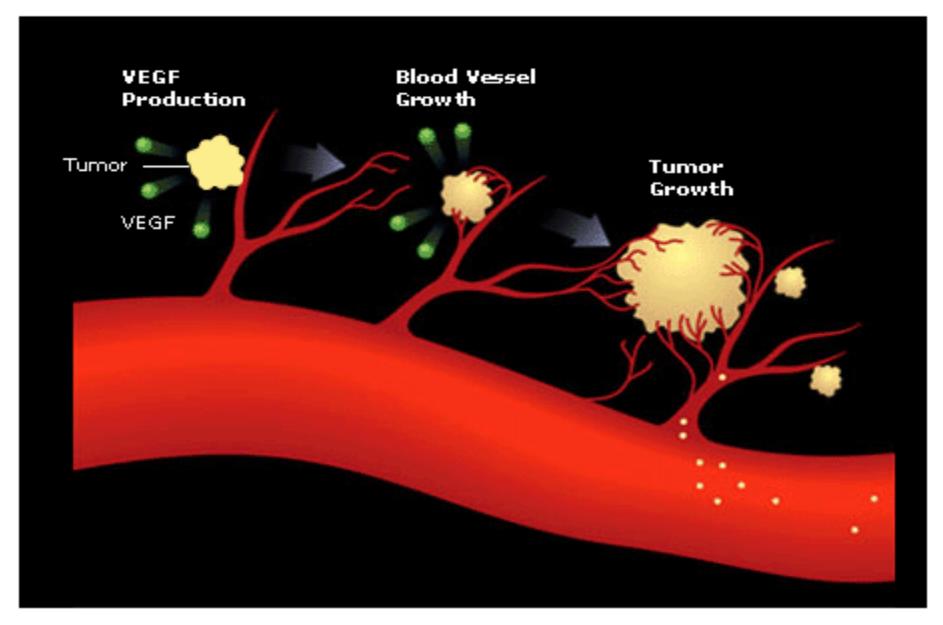
#### A. Unfractionated heparin: ÇH<sub>2</sub>OR<sub>1</sub> CH2OR1 COOR<sub>3</sub> COOR3 $OR_1$ OR<sub>1</sub> ~OH OR<sub>1</sub> OR<sub>1</sub> ÒR<sub>1</sub> NHR<sub>2</sub> NHR<sub>2</sub> n = 20 - 35, R1 = H or SO3, R2 = H or Ac or SO3, R3 = H or Na\* **LMWHS** B. Tinzaparin: COOR<sub>3</sub> CH2OR1 CH<sub>2</sub>OR<sub>1</sub> COOR<sub>3</sub> OR<sub>1</sub> $OR_1$ OR<sub>1</sub> $OR_1$ OH NHR<sub>2</sub> NHR<sub>2</sub> ÒR₁ ÓR<sub>1</sub> n = 4 - 10, R<sub>1</sub> = H or SO<sub>3</sub>, R<sub>2</sub> = H or Ac or SO<sub>3</sub>, R<sub>3</sub> = H or Na<sup>+</sup> C. NAC heparin: HO COOR3 COOR<sub>3</sub> CH2OR1 COOR3 OR1 ÓН OR<sub>1</sub> NHR<sub>2</sub> ÓR1 R1 = H or SO3, R2 = H or Ac or SO3, R3 = H or Na+

Figure 1. Chemical structure. Molecular structure of: (A), unfractionated heparin; (B), Tinzaparin; and (C), NAC heparin.

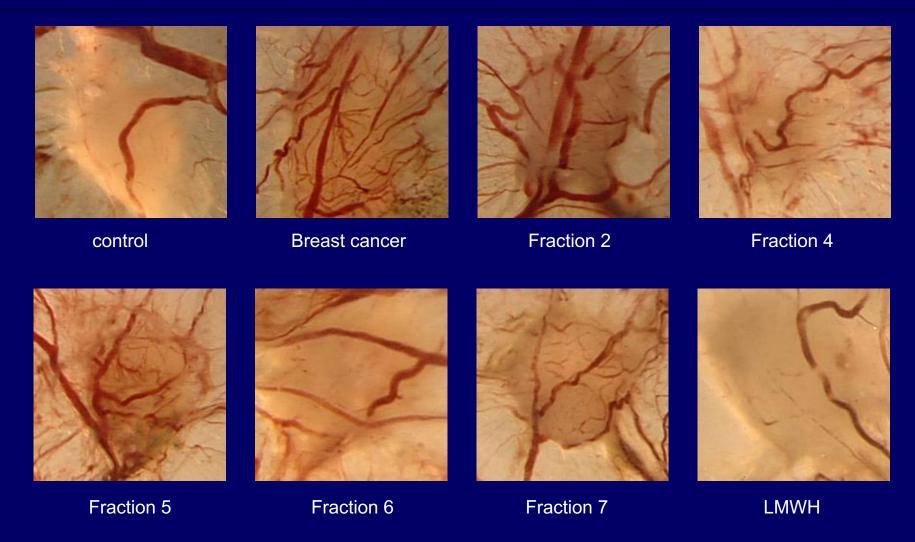


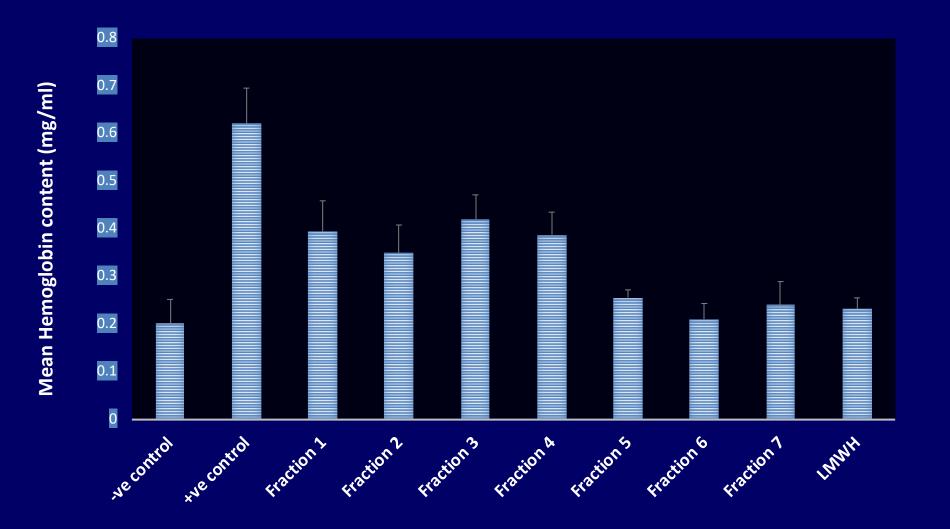
Time-schedule for camel urine fraction collection (Fractions 1-7). An aliquot of 30  $\mu$ l camel urine was injected onto a normal (NH3) HPLC column and eluted with 95% acetonitrile at 1 ml/min. The fractions were collected on the time-schedule. The fractions at same time period from three injection (90  $\mu$ l of urine in total) were pooled and dried by lyophilization.

## Angiogenesis



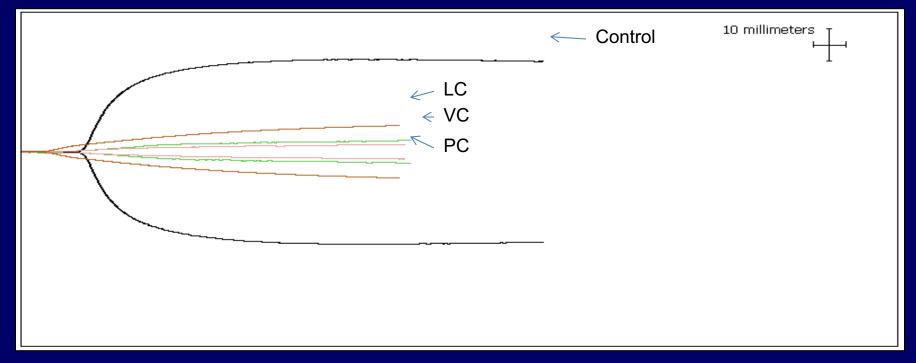
# Representative illustration for the effect of HPLC-SEC separated camel urine fractions (1-7) versus LMWH on human chemo-resistant breast cancer cells (MCF7-Doxorubicin resistant) tumor angiogenesis in the CAM model





Effect of HPLC-SEC separated camel urine fractions (1-7) on human chemo-resistant breast cancer cells (MCF7-Doxorubicin resistant) tumor angiogenesis in the CAM model

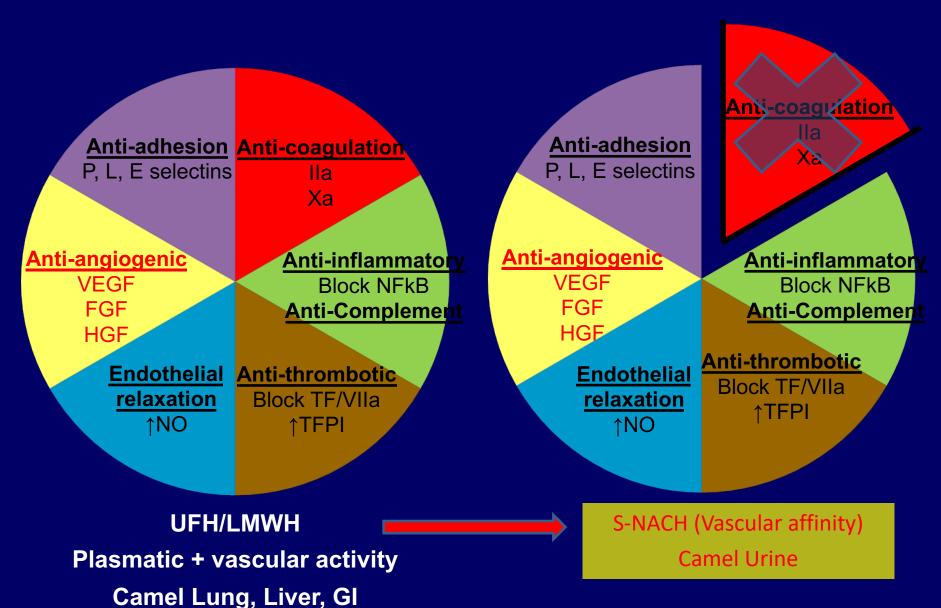
### Effect of Camel Urine Fractions on human Clot Kinetic Using TEG

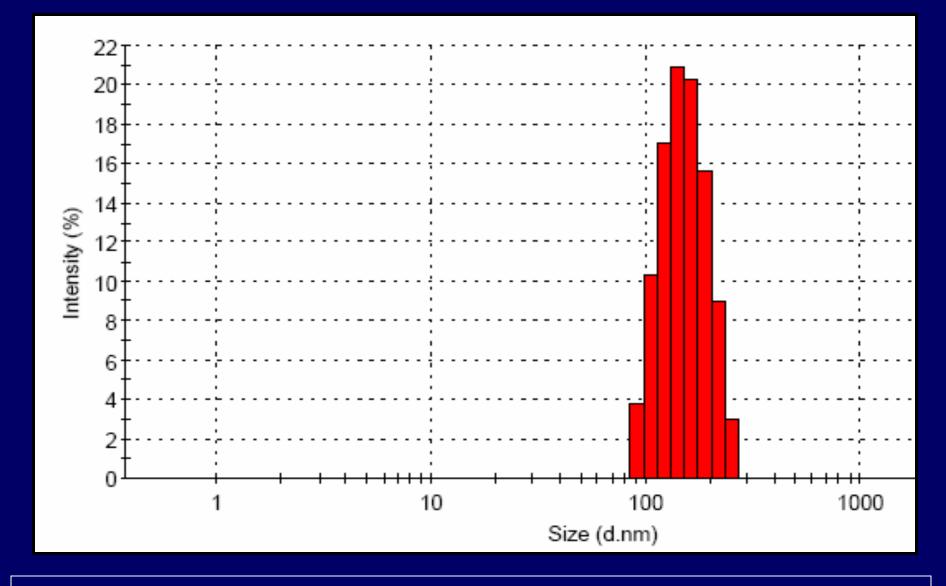


|                      | R    | MA   | angle |
|----------------------|------|------|-------|
| Control              | 9.6  | 55.4 | 59.1  |
| Lactating Camel (LC) | 14.7 | 4.8  | 2.9   |
| Virgin Camel (VC)    | 16.1 | 2.4  | 2.1   |
| Pregnant Camel (PC)  | 5.8  | 10.7 | 12.5  |

Illustrate the anticoagulant activity of GAGs camel bio products in various camel urine

## Multiple Pathways Targeted by UFH/LMWH and S-NACH





DLS data showing the size distribution of Camel Lactoferrin nanoparticles encapsulating the camel derived GAG: NACHs, chondroitin / dermatan sulfate (average size~150nm).

### References US Patents

*Mousa;* SA Al Haider; A, Abdelgader; A, Aldahmash; A, ➤ Almomen; A: Methods and compositions of camel derived products. *US Patent 9,770,419; September 26, 2017*.

Mousa, SA: Composition and method for sulfated non- • anticoagulant low molecular weight heparins in cancer and tumor metastasis. *US Patent 9,572,831; February 21, 2017.* 

Mousa SA: Composition and method of use for combinations of anti-viral protease, polymerase inhibitors and natural bioactive compounds in the treatment of hepatitis C infection. <u>US Patent</u> 10,046,005, August 14, 2018.

### References US Patents – Cont.

Mousa SA: Compositions and method for anti-sickling of red blood cells in sickle cell disease. *US Patent 9,822,190, November 2017* 

Mousa SA: Method and composition of glycosaminoglycan in sickle cell and vascular disorders. *US Patent 9,480,703; November 2016.* 

Mousa SA: Ocular Nanoformulation and method of use in angiogenesis-mediated disorders. **US Patent 9,655,862**; **May 2017**.

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### Literatures From Dr. Mousa Lab

Mousa SA et al: Sulfated non-anticoagulant heparin blocks Th2-induced asthma by modulating the IL-4/signal transducer and activator of transcription 6/Janus kinase 1 pathway. <u>J Transl Med. 2018 Sep 1; 16(1):243.</u>

Mousa SA et al: Anti-metastasis efficacy and safety of nonanticoagulant heparin derivative versus low molecular weight heparin in surgical pancreatic cancer models. *Int J Oncol. 2015 Mar; 46(3):1225-31.* 

Mousa SA et al: <u>Suppression of pancreatic cancer by sulfated non-anticoagulant low molecular weight heparin</u>. <u>Cancer Lett. 2014 Aug 1; 350(1-2):25-33.</u>

Mousa SA et al: Inhibitory effect of non-anticoagulant heparin (S-NACH) on pancreatic cancer cell adhesion and metastasis in human umbilical cord vessel segment and in mouse model. Clin Exp Metastasis. 2012 Jun; 29(5):431-9.

Mousa SA et al: Modulation of Sickle Red Blood Cell Adhesion and its Associated Changes in Biomarkers by Sulfated Non anticoagulant Heparin Derivative. <u>Clin. Appl.</u> <u>Thromb Hemost.</u> 2016 Apr; 22(3):230-8.

