Int. J. Morphol.,
43(3):978-985, 2025.

Histological and Histochemical Studies of the Bovine Endometrium During the Luteal Phase

Estudios Histológicos e Histoquímicos del Endometrio Bovino Durante la Fase Lútea

Mohamed E Alkafafy[1]; Salman Aloufi[1]; Manal Algethami[2] & Maram H. Abduljabbar[3]

ALKAFAFY, M. E.; ALOUFI, S.; ALGETHAMI, M. & ABDULJABBAR, M. H. Histological and histochemical studies of the bovine endometrium during the luteal phase. *Int. J. Morphol., 43(3)*:978-985, 2025.

SUMMARY: The study was conducted to check the validity of glycohistochemistry and the immunohistochemistry as valuable tools for the detection of the cyclic changes in the bovine endometrium during the luteal phase. Paraffin sections have been prepared from the uterine tissue specimens taken from 7 adult, clinically healthy, and apparently non-pregnant cows (*Bos taurus*). The histological findings revealed abundant populations of mast cells, especially within the subepithelial zone of stratum compactum and fewer numbers close to the endometrial glands in the stratum spongiosum, myometrium and perimetrium. The glycohistochemical findings indicated bindings sites within the luminal epithelium for GSA-1, DBA and WGA, but not for PNA. Yet, the glandular epithelium displayed bindings sites for all the four lectins. Some endometrial stromal cells and blood vessels exhibited binding sites only with GSA-1 and WGA. The immunohistochemical findings showed a strong immunoreactivity (IR) to angiotensin converting enzyme (ACE) within the apical surfaces of the luminal and glandular epithelia; reduced to moderate reactivity within the cytoplasm, vascular endothelium and periglandular solitary stromal cells. In conclusion, the topographic distribution of lectin binding sites and of the ACE-IR may represent useful tools to investigate the cyclic, hormone-controlled endometrial changes. This could be of value in understanding and interpretation of the pathophysiology of the bovine endometrium.

KEY WORDS: Cow; Endometrium; Endometrial glands; Mast cells; Lectins; ACE.

INTRODUCTION

The histological structure of the bovine uterus displays that it is built up of an outermost layer perimetrium, a middle myometrium, and an innermost layer endometrium. Endometrium, represents the uterine mucosa, which subjects to hormonal-related cyclic changes (Priedkalns & Leiser, 2006; Liebich, 2010; Espejel & Medrano, 2017). The endometrial stroma lies under the luminal epithelium and is made up from connective tissue containing the uterine glands. The endometrial stroma consists of a superficial, sub-epithelial zone called stratum compactum and a deep zone called stratum spongiosum. Whereas, the stratum compactum includes a densely organized array of connective tissue elements and immune cells, the stratum spongiosum displays a more loosely organized elements permeated by blood vessels, immune cells and endometrial glands (Priedkalns & Leiser, 2006; Espejel & Medrano, 2017).

Endometrium subjects to hormone-dependent cyclic changes, and thus passes through two stages: follicular (proliferative) and luteal (secretory) stages. The proliferative stage of the endometrial cycle is under the effect of estrogen, whereas the secretory stage is under the effect of progesterone (Espejel & Medrano, 2017). The uterine glands exist in the endometrial stroma. The endometrial glands belong to the simple, tubular, and branched glandular category. They produce the histotrophic secretion (Gray *et al*., 2001; Welsch & Sobotta, 2005; Salomon *et al*., 2005; Liebich, 2010; Espejel & Medrano, 2017). The glands are lined with a simple columnar epithelium of secretory and non-secretory ciliated cells (Priedkalns & Leiser, 2006; Espejel & Medrano, 2017). Whereas, the growth and branching of the glands is promoted by estrogen, the coiling and the secretory activity of the glands are progesterone-dependent (Priedkalns & Leiser, 2006).

It is worth noting that the secretory activity of the uterine glands is best studied using lectins or glycohistochemistry (Lee & Damjanov, 1985; Bychkov &

[1] Department of Biotechnology, College of Science, Taif University, Saudi, Saudi Arabia.
[2] Self-dependent Scholar, Jeddah, Saudi Arabia.
[3] Department of Pharmacology and Toxicology, College of Pharmacy, Taif University, Taif, Saudi Arabia.
FUNDING. This research was funded by Taif University, Saudi Arabia, Project No. (TU-DSPP-2024-109).

Received: 2024-12-04 Accepted: 2025-01-29

Toto, 1986, 1987; Aoki *et al*., 1989; Jones & Aplin, 2009; Clark, 2015; Singh & Sharma, 2022). Lectins are prevalent proteins of non-immune origin, present in diverse living organisms, which specifically bind defined monosaccharides or oligosaccharides. Many lectins were identified, characterized and applied as valuable tools in studying glycoconjugates (Wu *et al*., 2009). Lectins are frequently applied to investigate the glycoconjugates in male (Calvo *et al*., 2000; Ha *et al*., 2003; Parillo *et al*., 2009; Schick *et al*., 2009; Alkafafy & Sinowatz, 2012; Alkafafy, 2022) and female (Carson, 2002; Jones & Aplin, 2009; Clark, 2015; Yu *et al*., 2020) reproductive systems in different species.

The mammalian uterus displays a high content of glycoconjugates, especially in the apical surfaces of epithelial cells and the endometrial secretions (Carson, 2002; Clark, 2015). Secretions of the endometrial glands increase significantly during the luteal phase of the reproductive cycle. These secretions possess high content of glycoconjugates that promote specific uterine functions, for instance implantation (Jones & Aplin, 2009; Clark, 2015). Glycans are abundantly expressed in the mammalian uterus, which subject to various hormone-controlled cyclic changes (Carson, 2002; Jones & Aplin, 2009). Glycosylation modifies the molecular and functional characteristics of glycoproteins, which is closely related to many physiological processes including implantation and placentation. During implantation, uterine endometrium transforms into a receptive status to accept the embryo. This may be attributed to N-glycosylation of uterine endometrium (Yu *et al*., 2020). The renin-angiotensin-aldosterone system (RAAS) is a peptidergic system with endocrine capacities (Paul *et al*., 2006). Angiotensinogen is split by renin to form angiotensin I (ANG I), which is then activated into Angiotensin II (ANG II) by angiotensin converting enzyme (ACE) (Paul *et al*., 2006; Uehara *et al*., 2013). ANG II exerts its biological effects via interaction with specific high-affinity receptors existing on the surface of target cells (Forrester *et al*., 2018). ANG II is not only a potent vasoconstrictor but may also be involved in the regeneration of new blood vessels (Ahmed *et al*., 1995). It may play a critical role in the control of uterine vascular bed and in the regeneration of the endometrium, acting as an angiogenic and mitogenic mediator (Hagemann *et al*., 1994; Paul *et al*., 2006; Yart *et al*., 2021).

There are many histochemical and immunohistochemical studies that exhibit special concern to the cyclic changes in the endometrium in woman. Yet, similar studies display relative scarcity in the livestock. Thus, the current work aims to use both glycohistochemistry and immunohistochemistry to shed light on the cyclic morphological changes in the bovine endometrium during the luteal phase.

MATERIAL AND METHOD

Animals and tissues. The uterine tissue specimens were taken from 7 adult (average age 3 years), clinically healthy, cows (*Bos taurus*) slaughtered at the local abattoir in Cairo, Egypt. Specimens were taken immediately after slaughter.

Conventional Histological Studies. Specimens of uterine tissues were subjected to fixation in neutral buffered formalin, dehydration in ascending grades of ethanol, clearing in xylene, embedding in paraffin wax and sectioning into 5 µm thick sections. Tissue sections were mounted on coated glass slides. Sections were stained with hematoxylin and eosin, as well as with Alcian and Toluidine blue as described by Bancroft *et al*. (1996).

Lectin histochemistry. Distribution of glycoconjugates in the uterine tissues was investigated using four different fluorescein isothiocyanate (FITC) conjugated lectins (Sigma-Aldrich, Munich, Germany). Dewaxed and rehydrated sections were subjected to lectin histochemical procedures as described by Alkafafy & Sinowatz (2012). Controls were performed by either substitution of the lectins with buffer, or by preincubation of the lectins with the corresponding hapten sugar inhibitor.

Immunohistochemistry. For immunostaining, uterine tissue sections were dewaxed and rehydrated. The activity of the endogenous peroxidases was stopped by adding 1 % hydrogen peroxide (H_2O_2) for 15 min. Then the antigens were retrieved using heat conducted by a microwave oven (700 watt). Thus, sections were immersed in Tris/EDTA buffer (pH 9) and heated for 10 min. Blocking of non-specific bindings in sections by 5 % bovine serum albumin (BSA) in phosphate buffered saline (PBS) for an hour. Incubation of sections in humidified chamber with the specific primary antibodies (Rabbit recombinant monoclonal anti-ACE, ab254222-Abcam;1:4000) for 1 h, at room temperature. The sections were washed by PBS and incubated with the specific secondary antibody (Biotinylated pig anti-rabbit IgG, Dako, Hamburg; 1:300) for 30 min at room temperature. The sections were washed by PBS for 10 min. Then the secondary antibody was detected with Vectastain ABC kit (Vector Laboratories Inc., USA), then washed by PBS and the color was developed using DAB reagent (Sigma-Aldrich, St. Louis, MO, USA). Nuclei was stained by immersing the sections in hematoxylin as a counterstained, for 30 s.

Negative controls were applied by omitting the primary or secondary antisera or the ABC reagent, and confirmed that no positive staining. Positive controls were conducted following the manufacturers' instructions.

Scoring and photomicrography. Lectin-stained and immunostained uterine tissues and their controls were evaluated with a semi-quantitative subjective scoring performed by three independent observers, blind to the experimental design. Photomicrographs for general histology and immunohistochemistry were taken using an imaging system, assembled from a light microscope (Leica DM LB, Wetzlar, Germany) and a digital camera (Leica EC3, Heerbrugg, Switzerland). Lectin-stained sections were examined by using a Dialux 20 fluorescent microscope (Leitz GmbH, Wetzlar, Germany) and the photos were taken using Kodak Elite 400 film.

RESULTS

Histological findings. The histological findings showed that the bovine uterus is formed of the typical three layers: endometrium, myometrium and perimetrium. The bovine endometrium during the luteal (secretory) phase displayed a luminal epithelium of simple columnar or pseudostratified columnar type and an endometrial stroma of a superficial stratum compactum highly infiltrated with mast cells (Fig. 1a, 1b), and a deep stratum spongiosum manifested by several profiles of crossly cut endometrial glands that may also be surrounded by mast cells (Fig. 1c, 1d). Mast cells were not infrequent within the myometrium and perimetrium (Fig. 1c).

Glycohistochemical findings (Table I). The bovine secretory endometrium displayed a variable reactivity towards the different lectins applied. This variation included both the topographical distribution of binding sites and the intensity of the binding. The luminal epithelium expressed a moderate binding with DBA and GSA-1,

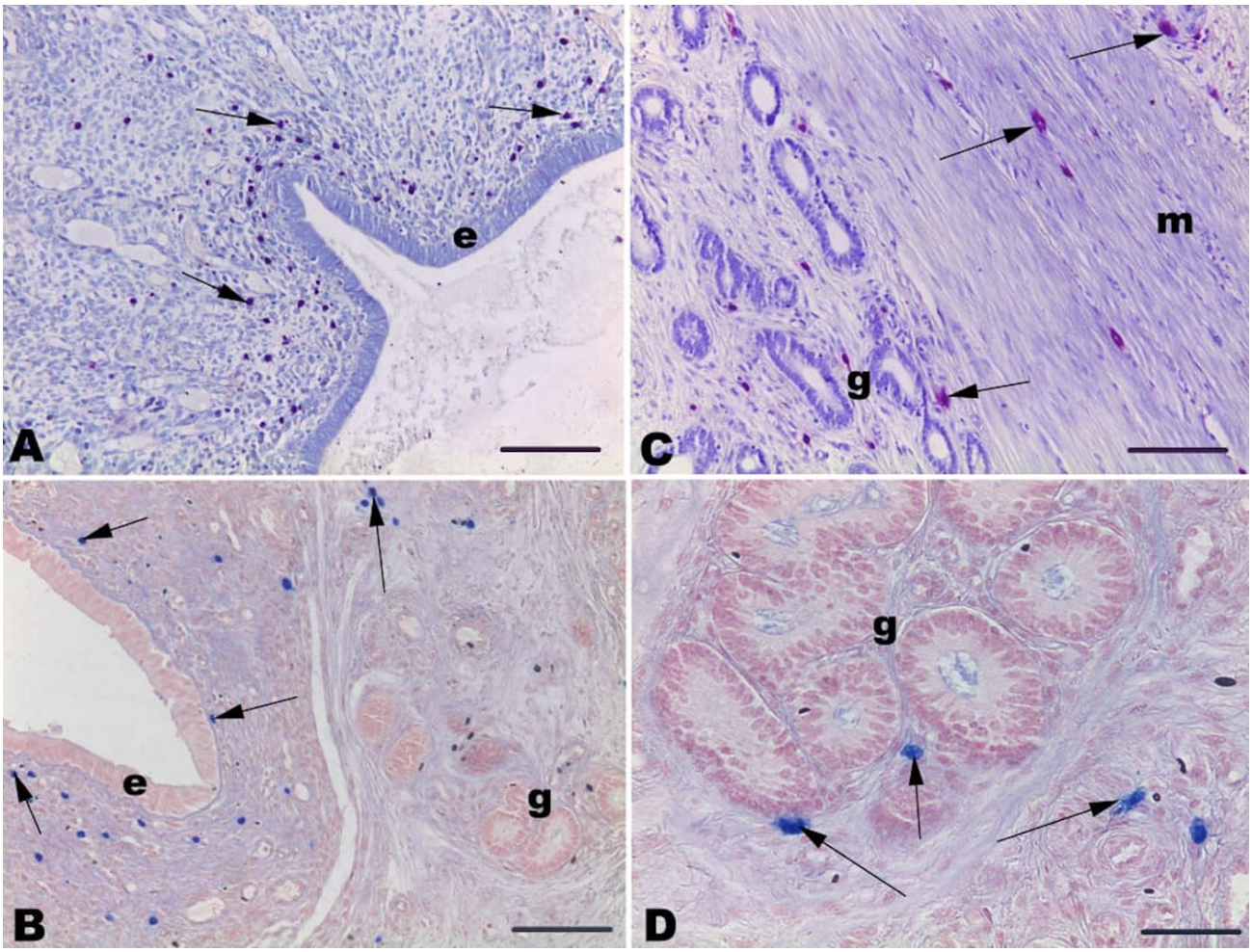

Fig. 1. Toluidin blue-stained and Alcian blue-stained sections of bovine uterus: (a) toluidine blue-stained mast cells (arrows) within the stratum compactum of the endometrial stroma; (b) Alcian blue-stained mast cells (arrows) within the stratum compactum of the endometrial stroma; (c) Toluidin blue-stained mast cells (arrows) within the stratum spongiosum of the endometrial stroma and the myometrium; (d) Alcian blue-stained mast cells (arrows) around the endometrial gland within the stratum spongiosum of the endometrial stroma. Surface epithelium (e), endometrial glands (g), and myometrium (m). Scale bars: 100 μm (a, b, and c) and 50 μm (d)

particularly in the apical surface. This binding intensity was reduced to weak (WGA) or totally vanished out (PNA). The cytoplasm of the cells in the luminal epithelium showed negative (PNA), weak (DBA, WGA), and moderate (GSA-1) binding. On the other hand, the basal portions of the luminal epithelium exhibited negative (DBA, PNA), negative to weak (WGA), and moderate (GSA-1) binding (Fig. 2).

Table I. Distribution of lectin-binding sites in the bovine endometrium.

Lectins	Luminal epithelium			Endometrial glands			Endometrial stroma	
	Ap	Cyt.	B	Ap	GZ	B	BVs	Cells
GSA-1	++	++	++	+++	+	+	+/++	+/++
DBA	+	+	-	+++	±	±	-	-
PNA	±	±	±	+/++	±	±	-	-
WGA	+	+	±	+++	+	+	+	+

Ap; Apical surface, B; Basal portion, Cyt; Cytoplasm; GZ; Golgi zone, BVs; Blood vessels. Negative (-), negative to weak (±), weak (+), weak to moderate (+/++), moderate (++), strong (+++) labeling

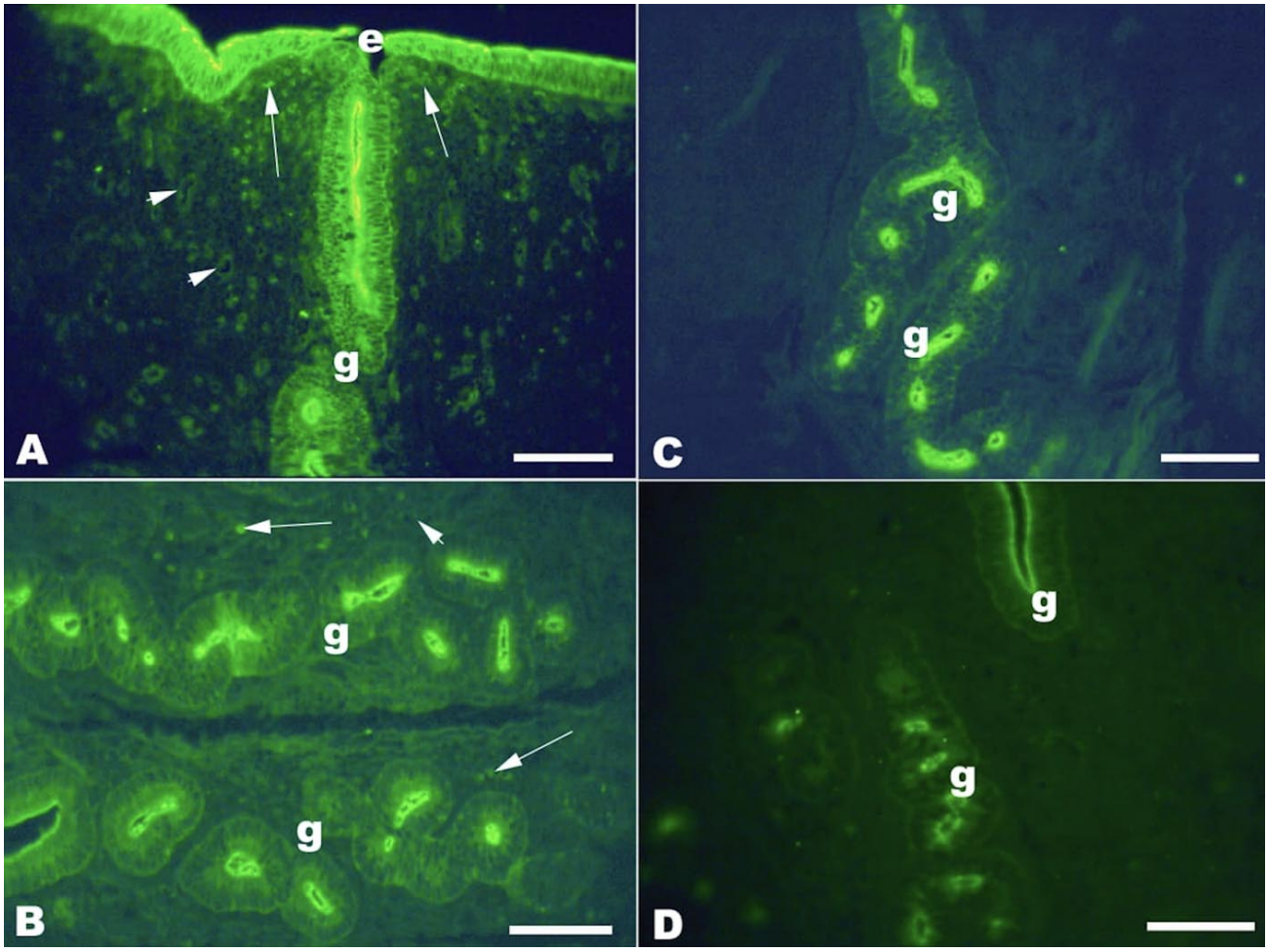

Fig. 2. Distribution of binding sites of FITC-lectins in the bovine uterus: (a) GSA-1-binding sites were strong (apical surface of the glandular epithelium), moderate (luminal epithelium), and weak to moderate (blood vessels and some scattered stromal cells); (b) WGA-binding sites were strong (apical surface of the glandular epithelium) and moderate in the luminal epithelium and the stromal blood vessels and cells; (c) DBA-binding sites were strong (apical surface of the glandular epithelium), weak to moderate (luminal epithelium), and negative (blood vessels and some scattered stromal cells); (d) PNA-binding sites were negative (blood vessels and stromal cells), negative to weak (Golgi zone), and weak to moderate (glandular epithelium). Surface epithelium (e), and endometrial glands (g). Scale bars: 50 μm.

The luteal phase endometrial stroma exhibited mostly negative reactivity with the different lectins. However, the blood vessels and some scattered stromal cells expressed binding ranged from negative (DBA, PNA), weak (WGA), and weak to moderate (GSA-1) binding (Fig. 2). On the other hand, the glandular epithelium also showed an inconstant reactivity with the different lectins. The binding was the highest within the apical surface and portion of the cells constituting the glandular epithelium, especially with GSA-1, DBA and WGA that exhibited a strong reactivity. Yet, this binding was relatively reduced into weak to moderate reactivity with PNA. The Golgi zone of the glandular epithelium displayed a variable reactivity ranged from weak to negative (DBA, PNA) to weak (GSA-1, WGA) binding. Likewise, the basal portions of the glandular epithelium exhibited a binding pattern similar to that revealed by the Golgi zone (Fig. 2).

ACE immunoreactivity (Table II). The endometrial luminal epithelium exhibited a variable ACE immunoreactivity (ACE-IR), which was strong in the apical surface reduced to moderate in the cytoplasm (Fig. 3a, 3b). The endometrial glands showed a similar pattern of ACE-IR, especially the apical surface of the glandular epithelium, which expressed a strong reactivity (Fig. 3a-d). The cytoplasm of the glandular epithelium displayed an inconsistent reactivity, ranged from negative (in the non-ciliated cells) to a moderate (in the ciliated cells) ACE-IR (Fig. 3c, 3d). On the other hand, the nuclei of the ciliated cells showed a moderate to strong ACE-IR (Fig. 3c, 3d). Apart from the moderately reactive vascular endothelial cells and some perivascular and periglandular stromal cells, the endometrial stroma exhibited mostly negative ACE-IR (Fig. 3c, 3d).

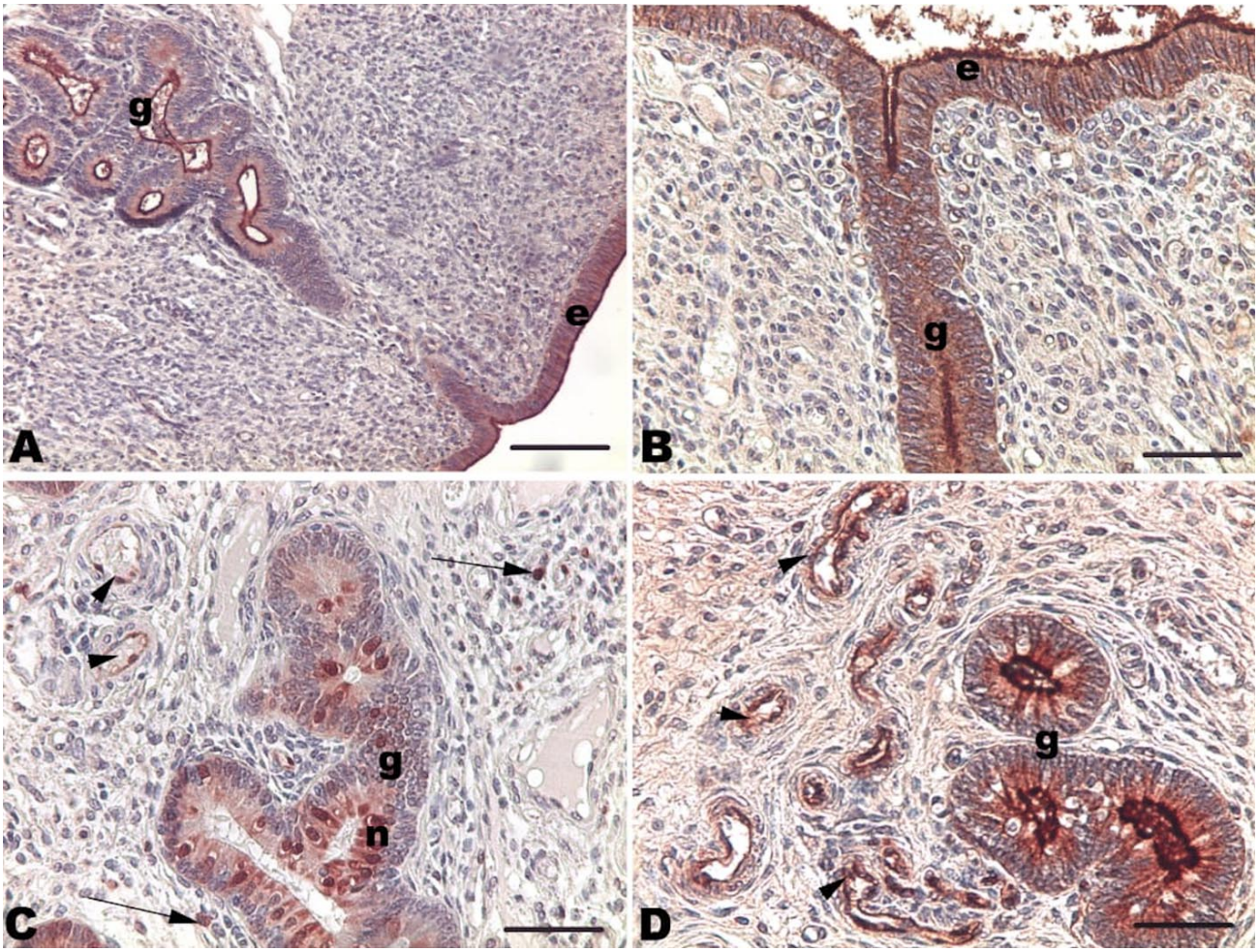

Fig. 3. ACE-immunostained bovine endometrium: (a) and (b) luminal and glandular epithelium presents moderate (in cytoplasm) to strong (in apical surfaces) ACE-IR; (c) and (d) the glandular epithelium displays ACE-IR ranges from strong (in apical surface), moderate to strong (in nuclei of ciliated cells), moderate (in cytoplasm of ciliated cells) to negative (in cytoplasm of non-ciliated cells). The endometrial stroma shows moderately reactive vascular endothelium (arrowheads) and periglandular stromal cells (arrows). Surface epithelium (e), and nuclei of ciliated cells (n) in the endometrial glands (g). Scale bars: 100 μm (a) and 50 μm (b, c, and d).

Table II. Distribution of Angiotensin converting enzyme (ACE)-binding sites in the bovine endometrium.

Item	Luminal epithelium			Endometrial glands			Endometrial stroma
	Ap. S.	Cyt.	Nuc	Ap. S.	Cyt.	Nuc	
LE	+++	++	-				
CC				+++	++	++/+	
NC				-	-	-	
VE							+/++
SC							+/++

LE; luminal epithelium, CC; ciliated cells, NC; non-ciliated cells, VE; vascular endothelium, SC; stromal cells, ApS; apical surface, Cyt; cytoplasm, Nuc; nucleus. Negative (-), weak to moderate (+/++), moderate (++), moderate to strong (++/+++) strong (+++) labeling

DISCUSSION

The current histological findings are consistent with previous studies that reported that the bovine uterine wall is made up of three layers: endometrium, myometrium and perimetrium (Priedkalns & Leiser, 2006; Liebich, 2010; Espejel & Medrano, 2017). Moreover, our findings display that the bovine endometrium during the luteal phase presents a simple, high columnar or pseudostratified columnar luminal epithelium and a stroma of a superficial stratum compactum highly infiltrated with mast cells, and a deep stratum spongiosum manifested by several profiles of crossly cut endometrial glands that are usually surrounded by mast cells. These findings go in line with previous reports, which showed that the endometrium at luteal stage is secretory and is under the influence of progesterone (Priedkalns & Leiser, 2006; Espejel & Medrano, 2017). It is worth mentioning that the secretory stage is concomitant with the existence of functional corpus luteum on the ovary and the secretion of progesterone. This microenvironment promotes the endometrium to reach maximum thickness, get lager blood vessels and present abundant and tortuous active glands exhibiting secretory capacity [(Liebich, 2010; Espejel & Medrano, 2017).

Regarding the mast cells that were abundant in the stratum compactum of the endometrial stroma and were not infrequent within the stratum spongiosum, myometrium and even in perimetrium; this was in agreement with previous findings in the bovine (Espejel & Medrano, 2017) and in the canine (Martins *et al*., 2020) uterus. Similar findings were also reported in other mammalian species including Syrian hamster (Brandon & Evans, 1983), human (Drudy *et al*., 1991), rat (Karaca *et al*. 2007) and goat (Karaca *et al*., 2009). Moreover, earlier studies showed that the there is a positive correlation between the progesterone levels and the numbers of mast cells in the uterus of woman (Milne *et al*., 2001) and bitch (Goericke-Pesch *et al*., 2010). On the other hand, a reduction in the numbers of mast cells in the uterus has been previously attributed to estrogens (Maraspin & Bo, 1971). Furthermore, Batth & Parshad (2000) proposed that the high release of histamine during the period of embryonic implantation is among the known functions of the mast cells in the uterus. Also, Espejel & Medrano (2017) reported that the presence of inflammatory and mast cells in the bovine endometrium may represent a defense against infections.

In the current study, the luminal epithelium (apical surface, cytoplasm, and basal portions) expressed a moderate binding with GSA-1 and DBA, but failed to express PNA-binding. On the other hand, the luteal phase endometrial stroma expressed weak to moderate GSA-1-binding, but failed to display binding with DBA or PNA. The binding with GSA-1 and DBA was the strongest (in the apical surface and apical portions) reduced to weak (in Golgi zone and the basal portions) of the glandular epithelial cells. Moreover, the glandular epithelium exhibited a PNA-binding pattern similar to that of GSA and DBA, but with much weaker intensity. The current findings were supported by earlier studies on the human endometrium (Lee & Damjanov., 1985; Bychkov & Toto, 1986, 1987), on the caprine endometrium (Singh & Sharma, 2022), and on the bovine endometrium (Caspe *et al*., 2021). Moreover, PNA has been considered the most remarkable marker of pregnancy-related changes in woman's endometrium (Bychkov & Toto, 1987).

Although some lectins have the specificity to the same sugar, they display different binding pattern. For example, both GSA-1, DBA and PNA are N-acetyl-galactosamine-binding lectins. Yet, they displayed obvious unevenness in their distribution pattern throughout the bovine endometrial compartments. This is in agreement with previous studies (Alkafafy, 2022). Consequently, lectins with corresponding specificity to a certain sugar can detect discrepancies in the organizational complexity of receptors (Kunz *et al.*, 1984). So, lectins with the same monosaccharide specificity do not necessarily link to the same glycoconjugates. This may be ascribed to the concept that the binding of a sugar with its specific lectin may be affected by numerous factors, for instance the impact of the neighboring sugars within the saccharide chain (Malmi & Söderström, 1988).

It is well-known that WGA binds selectively with its specific sugars that include β-N acetyl-D-glucosamine and α-N-acetyl neuraminic acid. It displayed a weak (in the luminal epithelial cells) to strong (in the glandular epithelial cells) binding. Also, its binding affinity was weak in the stromal compartments including blood vessels and stromal cells. The current findings go in line with earlier work on the caprine (Singh & Sharma, 2022), the human (Lee & Damjanov, 1985; Bychkov & Toto, 1986; Söderström, 1987; Aoki *et al*., 1989) endometrium.

Also, our findings were supported by those reported in caprine (Singh & Sharma, 2022) and in human (Söderström, 1987; Aoki *et al*., 1989) uterus, which indicated that binding intensity exhibited a positive correlation with progesterone. Additionally, the binding sites for the lectins may reveal a species-specific distribution pattern even in closely related species (Caspe *et al*., 2021).

The current immunohistochemical findings showed that endometrial luminal epithelium exhibited a variable ACE-IR, which was strong in the apical surface reduced to moderate in the cytoplasm. A similar pattern of ACE-IR was also recorded in the apical surface of the glandular epithelium; but not in the cytoplasm of the glandular epithelium exhibited an inconsistent ACE-IR, ranged from negative (non-ciliated cells) to a moderate (ciliated cells). Furthermore, the nuclei of the ciliated cells showed a moderate to strong ACE-IR. The present findings of ACE-IR in the bovine endometrium (luminal epithelium, glandular epithelium and vascular endothelium) during the luteal phase have been supported by earlier work on the ovine (Moeller *et al*., 1996), human (Li & Ahmed, 1997), bovine (Schauser *et al*., 2001) endometrium. Cyclic variations of ACE-IR have been reported with the highest expression in the late secretory phase (Li & Ahmed, 1997).

Apart from the moderately reactive vascular endothelial cells and some perivascular and periglandular stromal cells, the endometrial stroma exhibited mostly negative ACE-IR. The findings of the ACE-reactive mononuclear periglandular and perivascular stromal cells may be supported by the assumption of Schauser *et al*. (2001), about the solitary macrophage-like cells displaying intense renin immunoreactivity in the bovine uterus.

It is worth noting that ACE converts ANG I into its active form ANG II (Paul *et al*., 2006; Uehara *et al*., 2013). Also, an intense ANG II-immunoreactivity (ANG II-IR) has been reported in the glandular epithelium and in the perivascular stromal cells in the secretory human endometrium (Paul *et al*., 2006). Thus, cyclic changes in ANG II-IR as well as in the expression of angiotensin receptors indicates that angiotensin may play a critical role in the control of uterine vascular bed and in the regeneration of the endometrium, acting as an angiogenic and mitogenic mediator (Paul *et al*., 2006; Li *et al*., 2020).

In conclusion, the current findings of the glycohistochemical (topographic distribution of lectin binding sites) and immunohistochemical (ACE-IR) characteristics may represent useful tools to investigate the cyclic, hormone-controlled endometrial changes. This could be of value in understanding and interpretation of the physio-pathological changes in the bovine endometrium.

ACKNOWLEDGEMENTS. The authors extend their appreciation to Taif University, Saudi Arabia, for supporting this work through project number (TU-DSPP-2024-109).

ALKAFAFY, M. E.; ALOUFI, S.; ALGETHAMI, M. & ABDULJABBAR, M. H. Estudios histológicos e histoquímicos del endometrio bovino durante la fase lútea. *Int. J. Morphol., 43(3)*:978-985, 2025.

RESUMEN: El estudio se realizó para comprobar la validez de la glicohistoquímica y la inmunohistoquímica como herramientas valiosas para la detección de los cambios cíclicos en el endometrio bovino durante la fase lútea. Se prepararon secciones de parafina a partir de muestras de tejido uterino tomadas de 7 vacas adultas (*Bos taurus*), clínicamente sanas y aparentemente no gestantes. Los hallazgos histológicos revelaron abundantes poblaciones de mastocitos, especialmente dentro de la zona subepitelial del estrato compacto y menos números cerca de las glándulas endometriales en el estrato esponjoso, miometrio y perimetrio. Los hallazgos glicohistoquímicos indicaron sitios de unión dentro del epitelio luminal para GSA-1, DBA y WGA, pero no para PNA. Sin embargo, el epitelio glandular mostró sitios de unión para las cuatro lectinas. Algunas células del estroma endometrial y vasos sanguíneos exhibieron sitios de unión solo con GSA-1 y WGA. Los hallazgos inmunohistoquímicos mostraron una fuerte inmunorreactividad (IR) a la enzima convertidora de angiotensina (ECA) dentro de las superficies apicales de los epitelios luminal y glandular; reactividad reducida a moderada dentro del citoplasma, endotelio vascular y células estromales solitarias periglandulares. En conclusión, la distribución topográfica de los sitios de unión de lectinas y de la IR-ECA puede representar herramientas útiles para investigar los cambios endometriales cíclicos, controlados por hormonas. Esto podría ser valioso para la comprensión e interpretación de la fisiopatología del endometrio bovino.

PALABRAS CLAVE: Vaca; Endometrio; Glándulas endometriales; Mastocitos; Lectinas; ACE.

REFERENCES

Ahmed, A.; Li, X. F.; Shams, M.; Gregory, S. J.; Rollason, T.; Barnes, N. M. & Newton, J. R. Localization of the angiotensin II and its receptor subtype expression in human endometrium and identification of a novel high-affinity angiotensin II binding site. *J. Clin. Invest., 96(2)*:848-57, 1995.

Alkafafy, M. & Sinowatz, F. Prenatal development of the bovine epididymis: light microscopical, glycohistochemical and immunohistochemical studies. *Acta Histochem., 114(7)*:682-94, 2012.

Alkafafy, M. E. Application of lectins for detection of glycomic differences in the epididymal duct in water buffalo (Bubalus bubalis) and dromedary camel (Camelus dromedarius). *Int. J. Morphol., 40(3)*:662-71, 2022.

Aoki, D.; Kawakami, H.; Nozawa, S.; Udagawa, Y.; Iizuka, R. & Hirano, H. Differences in lectin binding patterns of normal human endometrium between proliferative and secretory phases. *Histochemistry, 92(3)*:177-84, 1989.

Bancroft, J. D.; Stevens, A. & Turner, D. R. Theory and Practice of Histological Techniques. 4th ed. London, Churchill Livingstone, 1996.

Batth, B. K. & Parshad, R. K. Mast cell dynamics in the house rat (*Rattus rattus*) ovary during estrus cycle, pregnancy and lactation. *Eur. J. Morphol., 38(1)*:17-23, 2000.

Brandon, J. M. & Evans, J. E. Changes in uterine mast cells during the estrous cycle in the Syrian hamster. *Am. J. Anat., 167(2)*:241-7, 1983.

Bychkov, V. & Toto, P. D. Lectin binding to normal human endometrium. *Gynecol. Obstet. Invest., 22(1)*:29-33, 1986.

Bychkov, V. & Toto, P. D. Histochemical study of lectin binding to gestational endometrium. *Int. J. Gynecol. Pathol., 6(1)*:66-72, 1987.

Calvo, A.; Pastor, L. M.; Bonet, S.; Pinart, E. & Ventura, M. Characterization of the glycoconjugates of boar testis and epididymis. *J. Reprod. Fertil., 120(2)*:325-35, 2000.

Carson, D. D. The glycobiology of implantation. *Front. Biosci., 7*:d1535-44, 2002.

Caspe, S. G.; Konrad, J. L.; Prando Moore, D.; Sala, J. M.; Lischinsky, L.; Campero, C. M. & Barbeito, C. G. A comparative pattern of lectin-binding in the endometrial glands of the uterus and placenta of healthy buffaloes and bovines at early gestation. *Biocell, 45(2)*:331-7, 2021.

Clark, G. F. Functional glycosylation in the human and mammalian uterus. *Fertil. Res. Pract., 1*:17, 2015.

Drudy, L.; Sheppard, B. L. & Bonnar, J. The mast cell and histamine concentration of the human post-menopausal uterus. *Eur. J. Obstet. Gynecol. Reprod. Biol., 42(1)*:39-42, 1991.

Espejel, M. C. & Medrano, A. Histological cyclic endometrial changes in dairy cows: an overview. *Dairy Vet. Sci. J., 2(1)*:555577, 2017.

Forrester, S. J.; Booz, G. W.; Sigmund, C. D.; Coffman, T. M.; Kawai, T.; Rizzo, V.; Scalia, R. & Eguchi, S. Angiotensin II signal transduction: an update on mechanisms of physiology and pathophysiology. *Physiol. Rev., 98(3)*:1627-738, 2018.

Goericke-Pesch, S.; Schmidt, B.; Failing, K. & Wehrend, A. Changes in the histomorphology of the canine cervix through the oestrous cycle. *Theriogenology, 74(6)*:1075-81, 2010.

Gray, C. A.; Taylor, K. M.; Ramsey, W. S.; Hill, J. R.; Bazer, F. W.; Bartol, F. F. & Spencer, T. E. Endometrial glands are required for preimplantation conceptus elongation and survival. *Biol. Reprod., 64(6)*:1608-13, 2001.

Ha, T. Y.; Ahn, M. J.; Lee, Y. D.; Yang, J. H.; Kim, H. S. & Shin, T. K. Histochemical detection of glycoconjugates in the male reproductive system of the horse. *J. Vet. Sci., 4(1)*:21-8, 2003.

Hagemann, A.; Nielsen, A. H. & Poulsen, K. The uteroplacental renin-angiotensin system: a review. *Exp. Clin. Endocrinol., 102(3)*:252-61, 1994.

Jones, C. J. P. & Aplin, J. D. Glycosylation at the fetomaternal interface: does the glycocode play a critical role in implantation? *Glycoconj. J., 26(3)*:359-66, 2009.

Karaca, T.; Yoruk, M. & Uslu, S. Distribution and quantitative patterns of mast cells in ovary and uterus of rat. *Arch. Med. Vet., 39(2)*:135-9, 2007.

Karaca, T.; Yörük, M.; Uslu, S.; Cetin, Y. & Uslu, B. A. Distribution of eosinophil granulocytes and mast cells in the reproductive tract of female goats in the preimplantation phase. *Vet. Res. Commun., 33(6)*:545-54, 2009.

Kunz, A.; Brown, D. & Orci, L. Appearance of Helix pomatia lectin-binding sites on podocyte plasma membrane during glomerular differentiation. A quantitative analysis using the lectin-gold technique. *Lab. Invest., 51(3)*:317-24, 1984.

Lee, M. C. & Damjanov, I. Pregnancy-related changes in the human endometrium revealed by lectin histochemistry. H*istochemistry, 82(3)*:275-80, 1985.

Li, S. Y.; Song, Z.; Yan, Y. P.; Li, B.; Song, M. J.; Liu, Y. F.; Yang, Z. S.; Li, M. Y.; Liu, A. X.; Quan, S.; *et al*. Aldosterone from endometrial glands is benefit for human decidualization. *Cell Death Dis., 11(8)*:679, 2020.

Li, X. F. & Ahmed, A. Compartmentalization and cyclic variation of immunoreactivity of renin and angiotensin converting enzyme in human endometrium throughout the menstrual cycle. *Hum. Reprod., 12(12)*:2804-9, 1997.

Liebich, H. G. *Funktionelle Histologie der Haussäugetiere und Vögel*. 5th ed. Stuttgart, Schattauer, 2010. pp.335-8.

Malmi, R. & Söderström, K. O. Lectin binding to rat spermatogenic cells: effects of different fixation methods and proteolytic enzyme treatment. *Histochem. J., 20(5)*:276-82, 1988.

Maraspin, L. E. & Bo, W. J. Effects of hormones, pregnancy and pseudopregnancy on the mast cell count in the rat uterus. *Life Sci. I, 10(2)*:111-20, 1971.

Martins, B. B.; Teixeira, N. S.; Teixeira, S. A. M. V.; Giannotti, J. G.; Nunes, L. C.; Freitas, P. M. C.; Machado-Neves, M. & Luz, M. R. Uterine secretory activity and histology of prepubertal female dogs in an animal model of partial ablation of endometrial glands development. *Pesq. Vet. Bras., 40(2)*:134-40, 2020.

Milne, S. A.; Rakhyoot, A.; Drudy, T. A.; Brechin, S.; Riley, S. C. & Critchley, H. O. Co-localization of matrix metalloproteinase-1 and mast cell tryptase in the human uterus. *Mol. Hum. Reprod., 7(6)*:559-65, 2001.

Moeller, I.; Chai, S. Y.; MacGregor, D. P.; Aldred, G. P. & Mendelsohn, F. A. Localization and quantitation of angiotensin AT1 and AT2 receptors in the pregnant and non-pregnant sheep uterus. *Regul. Pept., 61(3)*:213-8, 1996.

Parillo, F.; Verini Supplizi, A.; Macrì, D. & Catone, G. The ductus epididymis of the alpaca: immunohistochemical and lectin histochemical study. *Reprod. Dom. Anim., 44(2)*:284-94, 2009.

Paul, M.; Poyan Mehr, A. & Kreutz, R. Physiology of local renin-angiotensin systems. *Physiol. Rev., 86(3)*:747-803, 2006.

Priedkalns, J. & Leiser, R. *Female Reproductive System (Ch. 13).* In: Eurell, J. A. & Frappier, B. L. (Eds.). Dellmann's Textbook of Veterinary Histology. 6th ed. Hoboken, Wiley-Blackwel, 2006. pp.256-78.

Salomon, F. V.; Geyer, H. & Gille, U. *Anatomie für die Tiermedizin*. Stuttgart, Enke, 2005. pp. 383-8.

Schauser, K. H.; Nielsen, A. H.; Dantzer, V. & Poulsen, K. Angiotensin-converting enzyme activity in the bovine uteroplacental unit changes in relation to the cycle and pregnancy. *Placenta, 22(10)*:852-62, 2001.

Schick, B.; Habermann, F. & Sinowatz, F. Histochemical detection of glycoconjugates in the canine epididymis. *Anat. Histol. Embryol., 38(2)*:122-7, 2009.

Singh, P. & Sharma, R. K. Changes in surface morphology, lectin staining, and gene expression of caprine endometrium exposed to estradiol, progesterone, and mifepristone in vitro. *Iran. J. Vet. Res., 23(1)*:61-8, 2022.

Söderström, K. O. Lectin binding to formalin-fixed paraffin sections of human endometrium. *Int. J. Gynecol. Pathol., 6(1)*:55-65, 1987.

Uehara, Y.; Miura, S.; Yahiro, E. & Saku, K. Non-ACE pathway-induced angiotensin II production. *Curr. Pharm. Des., 19(17)*:3054-9, 2013.

Welsch, U. & Sobotta, J. *Lehrbuch Histologie.* 2nd ed. Munich,Urban & Fischer, 2005. pp.496-513.

Wu, A. M.; Lisowska, E.; Duk, M. & Yang, Z. Lectins as tools in glycoconjugate research. *Glycoconj. J., 26(8)*:899-913, 2009.

Yart, L.; Roset Bahmanyar, E.; Cohen, M. & Martinez de Tejada, B. Role of the uteroplacental renin-angiotensin system in placental development and function, and its implication in the preeclampsia pathogenesis. *Biomedicines, 9(10)*:1332, 2021.

Yu, M.; Qin, H.; Wang, H.; Liu, J.; Liu, S. & Yan, Q. N-glycosylation of uterine endometrium determines its receptivity. *J. Cell Physiol., 235(2)*:1076-89, 2020.

Corresponding author:
Dr. Mohamed Alkafafy
Department of Biotechnology College of Science
Taif University P. O. Box 11099
Taif 21944
SAUDI ARABIA

E-mail: m.kafafy@tu.edu.sa