مجلة كلية الإسراء الجامعة للعلوم الطبية

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وزارة التعليم العالي والبحث العلمي
دائرة البحث والتطوير

Republic of Iraq
Ministry of Higher Education & Scientific Research
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Date:

كلية الاسراء الجامعة / السيد العميد المحترم

م/ مجلة كلية الاسراء الجامعة للعلوم الطبية

السلام عليكم ورحمة الله وبركاته ...

أشارة الى كتابكم المرقم ع/١٩٥٠ في ٢١/ ١١/ ٢٠٢٠ بشأن اعتماد مجلتهم التي تصدر عن جامعتكم الموقرة واعتمادها لأغراض النشر والترقيات العلمية وتسجيلها ضمن موقع المجلات العلمية الاكاديمية العراقية ، حصلت موافقة السيد وكيل الوزارة لشؤون البحث العلمي بتاريخ ٢٠٢١/٢/١٤ على أعتماد المجلة المذكورة في الترقيات العلمية والنشاطات العلمية المختلفة الاخرى وتسجيل المجلة في موقع المجلات الاكاديمية العلمية العراقية ، وحسب ما جاء بأعمامنا المرقم ب ت ١٠٩٨٨/٤ في ٢٠١٩/١١/٢٤ **(تقرر اعطاء موافقة مؤقتة لمدة ٦ أشهر على ان يتم تزويدنا بالرقم المعياري الدولي المطبوع والالكتروني وانشاء موقع الكتروني للمجلة وبخلافة تلغى الموافقه وأعلامنا الاجراءات لاحقاً).**

للتفضل بالاطلاع وابلاغ مخول المجلة لمراجعة دائرتنا لتزويده باسم المستخدم وكلمة المرور ليتسنى له تسجيل المجلة ضمن موقع المجلات العلمية العراقية وفهرسة اعدادها ... مع التقدير.

السيد المدير العام المحترم

للتفضل بالتوقيع مع التقدير

د.هناء /المعاون

أ.د. غسان حميد عبدالمجيد
المدير العام لدائرة البحث والتطوير
٢٠٢١/٣/ ١

نسخة منه الى:
- مكتب السيد وكيل الوزارة لشؤون البحث العلمي / أشارة الى موافقة سيادته المذكورة أعلاه والمثبتة على اصل مذكرتنا المرقم ب ت م/٤ ١٠٩٣ في ٢٠٢١/٢/١٧ / للتفضل بالاطلاع ... مع التقدير .
- قسم المشاريع الريادية / شعبة المشاريع الالكترونية / للتفضل بالعلم واتخاذ مايلزم ... مع التقدير
- قسم الشؤون العلمية / شعبة التاليف والنشر والمجلات / مع الاوليات .
- الصادرة .

مهند ، أنس
٢٤/ شباط

وزارة التعليم العالي والبحث العلمي – دائرة البحث والتطوير – القصر الأبيض – المجمع التربوي – الطابق السادس
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تعليمات النشر

في مجلة كلية الإسراء الجامعة للعلوم الطبية

- تصدر كلية الاسراء الجامعة (مجلة كلية الاسراء الجامعة للعلوم الطبية) في مجلد سنوي يضم عددين.
- تقوم المجلة بنشر البحوث العلمية للباحثين في تخصصات العلوم الطبية التالية:
  - الطب العام وطب الأسنان
  - العلوم الصيدلانية
  - تقنيات المختبرات الطبية
  - تقنيات الاجهزة الطبية
  - التمريض
- يشترط في البحث المقدم للنشر أن لا يكون قد نشر أو أرسل لجهة أخرى للنشر .
تخضع البحوث المقدمة للنشر في المجلة للتقييم حسب الأصول العلمية المتبعة من قبل اثنين من المختصين في موضوع البحث ومن ذوي الكفاءة، وقد يستشار بثالث عند الضرورة مع حجب أسماء المقيّمين عند إرسال الملاحظات للباحثين.
- يلتزم الباحث بإجراء جميع التعديلات التي يراها المقيّمان ضرورية ويُرفض البحث إذا اتفق المقيّمان على رفضه، أو رفض من أحدهما وتعديلات جوهرية من الآخر، أو تعديلات جوهرية من كلا المقيّمين.
- يلتزم الباحث عند النشر في هذه المجلة بملىء استمارة التعهد الخاص يبين فيها ملكيته الفكرية للبحث وعدم نشره سابقاً في أي مجلة علمية أو مؤتمر علمي.
- تخضع البحوث المقدمة للنشر لتحديد نسبة الاستلال (الانتحال) Plagiarism باستعمال برنامج Turnitin.

- يعرض البحث قبل النشر للتدقيق من قبل مقيّم لغوي (اللغة العربية واللغة الانكليزية) ويجب على الباحث الالتزام بهذه التعديلات.

تلتزم المجلة بسياسة نشر تعكس التزامها بأخلاقيات البحث العلمي وبنود لجنة أخلاقيات النشر Committee of Publication Ethics

- تلتزم المجلة بجميع الضوابط الصادرة من وزارة التعليم العالي والبحث العلمي / دائرة البحث والتطوير الخاصة بالمجلات العلمية.
- تحتفظ هيئة التحرير بحقها بإجراء التعديلات الشكلية واللغوية اللازمة.
- تحتفظ هيئة التحرير بحقها في عدم نشر أي بحث دون إبداء الأسباب وتعتبر قراراتها نهائية.
- لا ترد البحوث لأصحابها سواء قبلت للنشر أو لم تقبل.
- يزود صاحب البحث بنسخة ورقية واحدة من العدد الذي نشر فيه بحثه.

شروط النشر

1. يطبع البحث بواسطة الحاسوب بمسافات مفردة بين الاسطر وبحجم خط 12 ونوع (Simplified Arabic)، اما العنوان باللغتين العربية والانكليزية فيكون بحجم خط 14 شريطة ألا يزيد عدد صفحاته عن 15 صفحة بما في ذلك الجداول والأشكال والمراجع وعلى وجه واحد على ورق قياس A4 مع ترك هامش في حدود 2 سم من الاعلى والاسفل وهامش بحدود 3 سم من الجانبين الايمن والايسر.
2. لا يفضل نشر البحوث من قبل رئيس وأعضاء هيئة التحرير في المجلة سواء كان البحث منفرداً أو مشتركاً.
3. يقدم البحث بثلاث نسخ ورقية ونسخة إلكترونية بعد قبول البحث للنشر، يسلم البحث بشكله النهائي مطبوعاً **بالنظام الاعتيادي** بمسافة منتظمة لكافة الصفحات عدا الصفحة الأولى **التي تتضمن عنوان البحث وأسماء الباحثين وعناوينهم والبريد الإلكتروني للباحث الأول باللغتين العربية والإنكليزية** وعلى قرص مدمج CD ببرنامج Microsoft Word 2010 .
4. تقبل البحوث باللغتين العربية والإنكليزية ويفضل كتابة البحث باللغة الإنكليزية.

دليل المؤلف Author Guidelines

أدناه الشروط والمتطلبات الواجب مراعاتها من قبل الباحث للنشر في هذه المجلة بشرط أن لا يكون البحث قد نشر أو سينشر في أية مجلة علمية أخرى ولم يمضِ على إنجازه أكثر من أربع سنوات.

1. يجب أن يكون عنوان البحث موجزاً قدر الإمكان ومعبر عن البحث.
2. أسماء الباحثين: تكتب أسماء الباحثين وعناوين عملهم بصورة واضحة مع البريد الإلكتروني للباحث الأول.
3. **يجب أن يتضمن المستخلص موجزاً واضحاً عن البحث مكون من 250-300 كلمة متبوعاً بكلمات مفتاحية 4-6. إذا كان البحث باللغة العربية فيكون المستخلص متبوعاً بالكلمات المفتاحية أولاً، ثم المستخلص متبوعاً بالكلمات المفتاحية باللغة الإنكليزية ثانياً والعكس صحيح.**
4. **المقدمة:** تتضمن مراجعة المعلومات وثيقة الصلة بموضوع البحث الموجودة في المصادر العلمية وتنتهي المقدمة بأهداف الدراسة وأساسها المنطقي.
5. **المواد وطرائق العمل:** تذكر طرائق العمل بشكل مفصل إن كانت جديدة، أما إذا كانت منشورة فتذكر بشكل مختصر مع الإشارة للمصدر، يستعمل النظام العالمي للوحدات Standard International of Units (S.I.Us) بكتابة الوحدات فضلاً عن استخدام مختصرات المصطلحات العلمية المعتمدة عالمياً، على أن تكتب بشكل كامل في أول مرة ترد في النص.
6. **النتائج والمناقشة:** تعرض بشكل موجز وهادف وبنظام متوالي وتعرض النتائج بأفضل صورة معبرة وتوضع الجداول والأشكال في أماكنها المخصصة بعد الإشارة إليها في النتائج.
7. يستعمل نظام الأرقام العربية وهكذا في البحوث المرسلة للنشر وتمثل مناقشة النتائج تعبيراً موجزاً عن النتائج وتفسيراتها.
8. تكون كتابة المصدر في **قائمة المصادر** متضمنة الآتي: اسم أو أسماء الباحثين، سنة النشر وعنوان البحث كاملاً واسم المجلة ورقم المجلد والعدد وعدد الصفحات، مثال:

حمزة، عصام شاكر و جارالله، عزيز لطيف ورشيد، فرقد عبدالله وسلمان، سرحان علي (2018)، تقدير مستويات الزئبق في مصل دم مستخدمين لحشوات الأسنان. مجلة كلية الإسراء الجامعة، المجلد الأول\العدد الأول: 281-294.

9. المستخلص الإنكليزي يجب أن يكون وافياً ومعبراً عن البحث بصورة دقيقة، وليس بالضرورة أن يكون ترجمة حرفية للمستخلص العربي و**متبوعا بكلمات مفتاحية 4-6**.

دليل المقيّم Reviewer Guidelines

أدناه الشروط والمتطلبات الواجب مراعاتها من قبل المقيم للبحوث المرسلة للنشر في هذه المجلة

1. ملء استمارة التقويم المرسلة رفقة البحث المطلوب تقييمه بشكل دقيق وعدم ترك أي فقرة بدون إجابة.
2. على المقيّم التأكد من تطابق وتوافق عنوان البحث باللغتين العربية والإنكليزية وفي حالة عدم تطابقهما اقتراح العنوان البديل.
3. أن يبين المقيّم هل أن الجداول والأشكال التخطيطية الموجودة في البحث وافية ومعبرة.
4. أن يبين المقيّم هل أن الباحث اتبع الأسلوب الإحصائي الصحيح.
5. أن يوضح المقيّم هل أن مناقشة النتائج كانت كافية ومنطقية.
6. على المقيّم تحديد مدى استخدام الباحث للمراجع العلمية الرصينة وحداثتها.
7. أن يؤشر المقيّم بشكل واضح على واحد من ثلاث اختيارات وهي:
   - البحث صالح للنشر بدون تعديلات.
   - البحث صالح للنشر بعد إجراء التعديلات.
   - البحث غير صالح للنشر.
8. يجب أن يوضح المقيّم بورقة منفصلة ما هي التعديلات الأساسية التي يقترحها لغرض قبول البحث.
9. للمقيّم حق طلب إعادة البحث إليه بعد إجراء التعديلات المطلوبة للتأكد من التزام الباحث بها.
10. على المقيّم تسجيل اسمه ودرجته العلمية وعنوانه وتاريخ إجراء التقييم مع التوقيع على استمارة التقييم المرسلة له رفقة البحث المرسل له للتقييم.

المصادر

1. تكتب الأسماء العلمية (اللاتينية) للنباتات والحيوانات وغيرها بحروف مائلة لتمييزها عن باقي النص وتسمى أسماء المواد الكيمياوية (المبيدات، الأدويــة..... الخ) بأسمائها العلمية وليست التجارية.
2. يشار إلى المصادر في متن البحث كما يلي:

اللقب او الاسم الثالث للمؤلف والسنة إذا كان البحث بإسم باحث واحد، وإذا كان مؤلفين فيذكران والسنة وإذا كانوا ثلاثة فأكثر فيذكر اسم الأول وآخرون والسنة.

3. ترتب المصادر حسب الصيغة العالمية (APA) وكما بالأمثلة المذكورة :

أ. بحث في مجلة.

اسم الباحث أو الباحثون، (السنة)، عنوان البحث، اسم المجلة، المجلد، العدد وصفحتي البدء والانتهاء للبحث.

ب. كتب.

اسم المؤلف أو المؤلفون، (السنة) عنوان الكتاب، الطبعة، دار النشر وعدد الصفحات.

ج. الرسائل والأطاريح الجامعية.

اسم الباحث، (السنة)، عنوان الرسالة أو الأطروحة، العنوان (الكلية والجامعة) وعدد الصفحات.

د. بحث في وقائع مؤتمر أو ندوة علمية.

اسم الباحث أو الباحثون، (السنة)، عنوان البحث، اسم المؤتمر أو الندوة العلمية، مكان الانعقاد، صفحتي البدء والانتهاء للبحث.

ترسل البحوث إلى مجلة كلية الإسراء الجامعة للعلوم الطبية على العنوان الآتي:

كلية الإسراء الجامعة – قسم التوثيق والنشر

بغداد \ العراق

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(تعهد الملكية الفكرية)

إني\إننا الباحث\الباحثين ..... صاحب\أصحاب البحث الموسوم

(.....

.....)

أتعهد\نتعهد بأن البحث قد أنجز من قبلي\قبلنا ولم ينشر في أي مجلة أخرى في داخل وخارج العراق وأرغب بنشره في مجلة (**مجلة كلية الإسراء الجامعة للعلوم الطبية**) في كلية الإسراء الجامعة.

التوقيع:

التاريخ:

(تعهد نقل حقوق الطبع والتوزيع)

إني\إننا الباحث\الباحثين ..... صاحب\أصحاب البحث الموسوم

(.....

.....)

أتعهد\نتعهد بنقل حقوق الطبع والتوزيع والنشر إلى مجلة (**مجلة كلية الإسراء الجامعة للعلوم الطبية**) في كلية الإسراء الجامعة.

التوقيع :

التاريخ :

المحتويات

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3.3.2 Application in synthetic mixture sample

The application of suggested method for the purpose of determination of CPA, SMX and SNA in its synthetic mixture samples was successfully accomplished. The results are presented in Table (7), which show excellent recovery values that indicate the absence of any probable interference from each other or the excipients.

Table 7: Proposed method for determination of CPA, SMX and SNA in synthetic mixture.

Samples	*Concentration* Taken (µg/ mL)*	*Concentration* fond (µg/ mL)*	*Recovery %*	*C.V* %*
CPA in synthetic mixture sample	20.00	20.90	102.25	0.003
	30.00	31.01	101.68	0.0024
SMX in synthetic mixture sample	20.00	20.55	102.75	0.0023
	30.00	30.67	102.23	0.0036
SNA in synthetic mixture sample	20.00	20.32	101.6	0.0013
	30.00	30.72	102.4	0.0028

***Average of three determinations.**

Conclusion

Reversed- Phase High- Performance Liquid Chromatography with fluorescent Detector and isocratic elution mobile phase analytical method was developed and validated for the separation and determination of chloramphenicol, Sulphamethoxazole and sulfanilamide in a triple mixture. The obtained results confirmed the ICH guidelines for check identification include linearity, range, precision, accuracy and specificity. The suggested method is characterized by the ability to separate chloramphenicol, Sulphamethoxazole and sulfanilamide in synthetic mixture and in pharmaceutical preparations.

3.3. Applications of this method

3.3.1 Application on pharmaceutical samples

Using the proposed chromatographic method, assay of CPA and SMX in its pharmaceuticals chloramphenicol capsule and eye drop Table (5), trimethoprim tablet and syrup were carried out Table (6). Satisfactory results were obtained for all two drugs in a good agreement with the label claims thereby suggesting that there is no interference from any of the excipients which are normally present in tablets

Table 5: Application of the developed method to the chloramphenicol concentration measurements in pharmaceutical Sample.

Sample	***Conc. taken (µg.mL-1)***	***Conc.* found (µg.mL-1)***	***Recovery %***	***C.V* %***
PHENICOL (eye drop) SDI- Iraq	20.00	19.77	98.85	0.072
Chloramphenicol Capsule SDI- Iraq	20.00	20.04	100.2	0.070

***Average of three determination**

Table 6: Application of the proposed method to the SMZ concentration measurements pharmaceutical preparations.

Sample	***Conc. taken (µg.mL-1)***	***Conc.* found (µg.mL-1)***	***Recovery %***	***C.V* %***
Metheprim syrup SDI, Iraq	20.00	18.108	90.54	1.055
Methoprim tablet SDI, Iraq	20.00	19.56	97.8	1.036

***Average of three determinations**

and 24 hours. No drug degradation was noticed and no change in chromatogram peak area was seen during the study.

3.2.3. Accuracy and Precision

The accuracy of the analysis method measures how close a value which is either agreeable as a normal true value or an agreeable reference value. On the other hand precision described the agreement among several results obtained in the same way (Rockville,2007).

The accuracy and precision of the method were established by analyzing the pure drug at three concentration levels each for five replicates. Average recovery and CV were calculated for each level.

The results are shown in Table (4) which were satisfactory and showed good accuracy and precision by the proposed methods.

Table 4: Evaluation of accuracy and precision to determine CPA, SMX and SNA by the suggested method.

Materials	*Conc. (µg/mL)*		*Relative Error %*	*C.V %*
	Taken	*Found **		
CPA	10	10.070	0.700	0.0060
	20	20.300	1.500	0.0010
	30	30.212	0.706	0.0005
SMX	10	10.091	0.910	0.0040
	20	20.225	1.125	0.0040
	30	30.311	1.036	0.0005
SNA	10	10.055	0.550	0.0050
	20	20.198	0.990	0.0020
	30	30.257	0.856	0.0005

***Average of three determinations.**

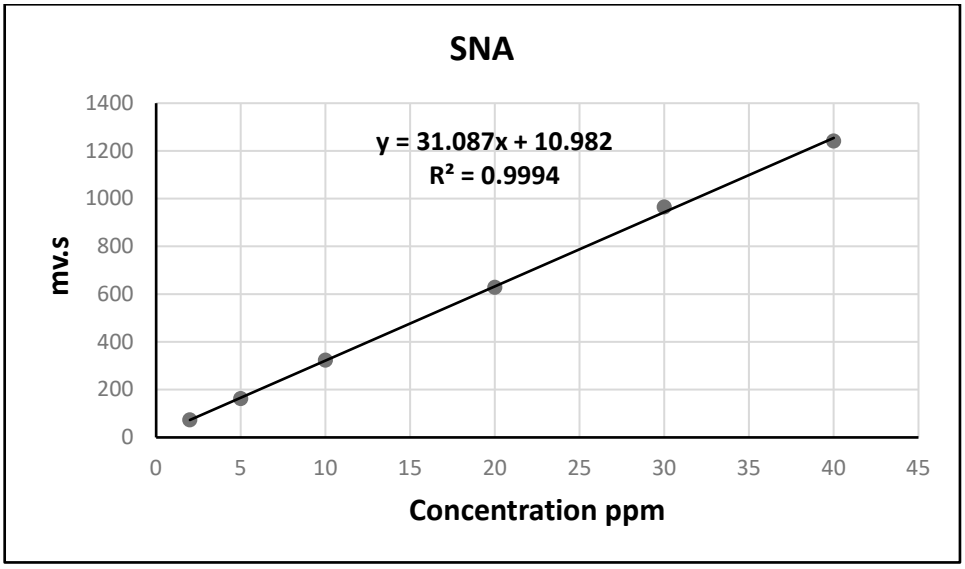

Fig. 8: Calibration curve was recorded between peak areas versus standard concentration (2, 5, 10, 20, 30, 40 ppm) for the determination of sulfanilamide under optimal conditions.

Table 3: Some statistical data to determine CPA, SMX and SNA via the recommended procedures.

	CPA	***SMX***	***SNA***
Regression equation	***y = 333.53x + 18.921***	***y = 105.85x - 26.047***	***y = 31.087x + 10.982***
Slop	333.53	105.85	31.087
R2	0.9996	0.9993	0.9994
Detection limit (µg/ mL)	0.016	0.044	0.184
Quantification limit (µg/ mL)	0.054	0.149	0.616

3.2.2. Solution Stability

Drug stability was checked using the proposed method by injecting fresh solutions of the substance to be analyzed using the system after 3, 12

A calibration curve was recorded between peak areas versus standard concentration Figs. (6, 7, 8). The results shown in Table (3) illustrate the linear results of this method over the finite run.

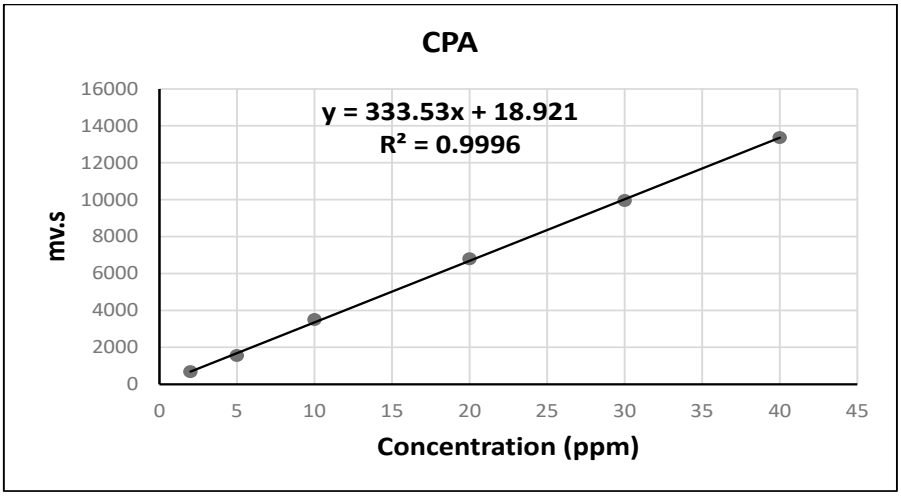

Fig. 6: Calibration curve was recorded between peak areas versus standard concentration (2, 5, 10, 20, 30, 40 ppm) for the determination of chloramphenicol under optimal conditions.

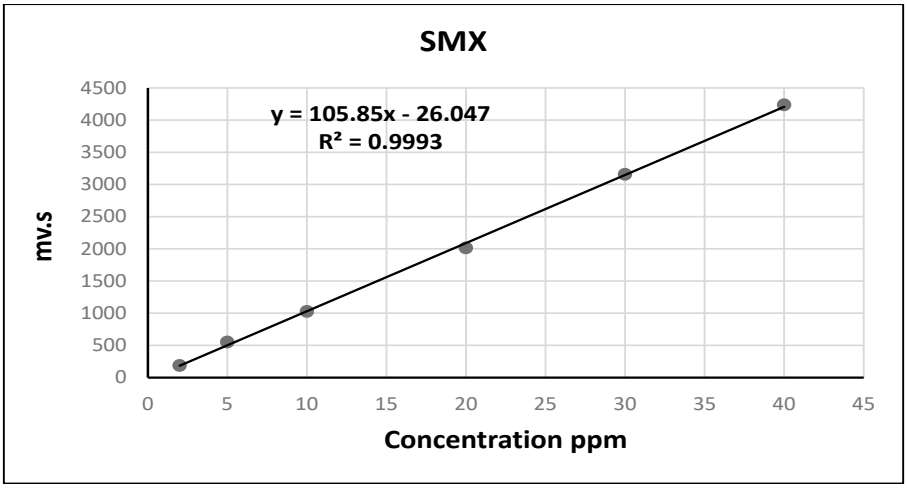

Fig. 7: Calibration curve was recorded between peak areas versus standard concentration (2, 5, 10, 20, 30, 40 ppm) for the determination of sulphamethoxazole under optimal conditions.

Table 2: Result for analysis of drugs mixture.

	Reten. Time [min]	Area [mV.s]	Height [mV]	Area [%]	Height [%]	W05 [min]	Compound Name
1	8.383	161.995	26.108	7.5	14.6	0.11	SNA (5 PPM)
2	8.983	1452.439	92.858	67.0	52.1	0.28	CAP (5 PPM)
3	10.500	553.437	59.407	25.5	33.3	0.16	SMX (5 PPM)
	Total	2167.871	178.373	100.0	100.0		

3.2. Method Validation

After developing the method, Validate the present analysis method, for chloramphenicol, sulfanilamide and sulphamethoxazole have been performed as per the ICH guidelines for check determination, including linearity, range, precision, accuracy and specificity (Validation of Analytical Procedure, 2005).

3.2.1. Linearity and Range

A linear relationship is the ability of a method to give analysis results that are immediately proportional to the concentration of the substance being analyzed within a gotten range. Range is the domain-inter the lower and upper part of the concentration of the substance under analysis whose estimation has been demonstrated with accuracy, linearity and precision utilizing the written method. At least five concentrations are needed with some specific minimal ranges. The correlation coefficient (R2) is the acceptance criteria for a linearity of at least 0.990 for least-squares mode for line analysis. Standard solutions were prepared by diluting a certain stock standard volume (100 ppm) to obtain a concentration (2, 5, 10, 20, 30, 40 ppm). Three runs were performed for each concentration.

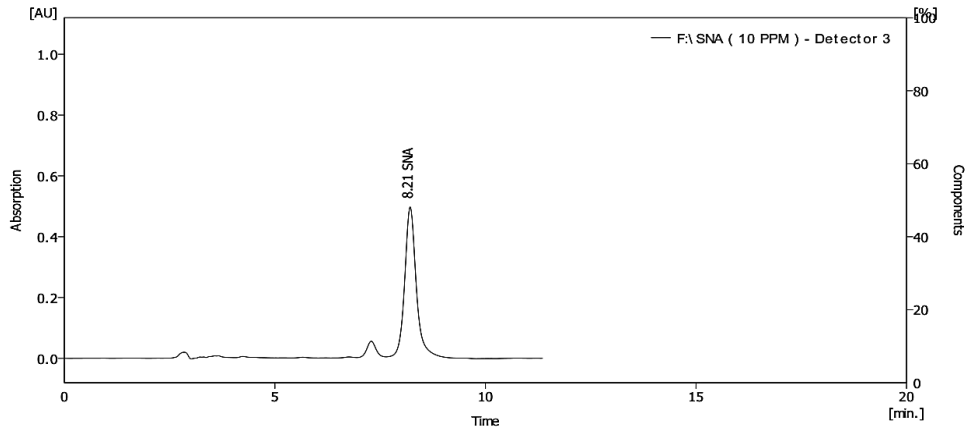

Fig. 4: Chromatogram for sulfanilamide analysis 10 ppm

At room temperature the column is kept during this study. It was noted that the separation process was not significantly affected by the change in column temperature. After this optimization, this method was used to separate chloramphenicol, sulfamethoxazole and sulfanilamide from each other in the same solution. Fig. (5). the result illustrate in Table (2) a suitable resolution has been obtained with a good separation.

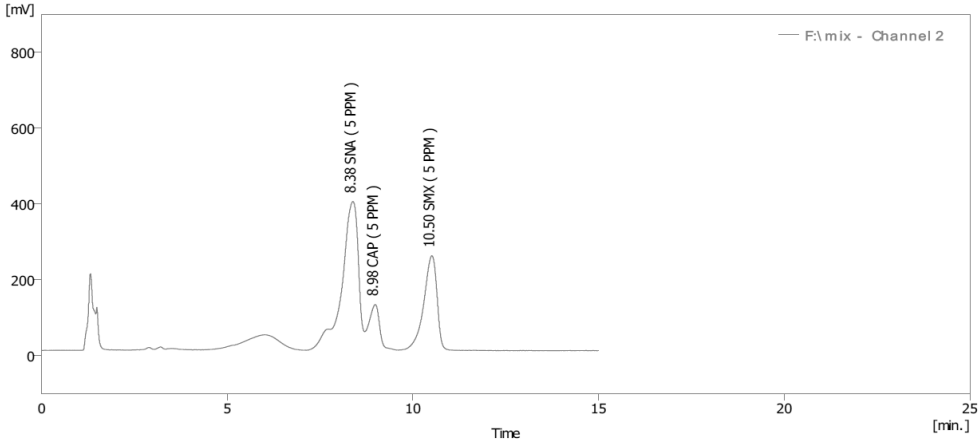

Fig. 5: Chromatogram for analysis of mixtures of SNA (5 ppm at 8.38 min), CPA, (5 ppm at 8.98 min) and SMX (5 ppm at 10.50 min).

Table 1. Isocratic elution mobile phase: A: methanol, B: D.W (2 % orthophosphoric acid)

Initial	A %	B %	Flow rate ml/min
0 – 6	50	50	1.0
6 – 8	60	40	0.7
9 – 14	30	70	0.7

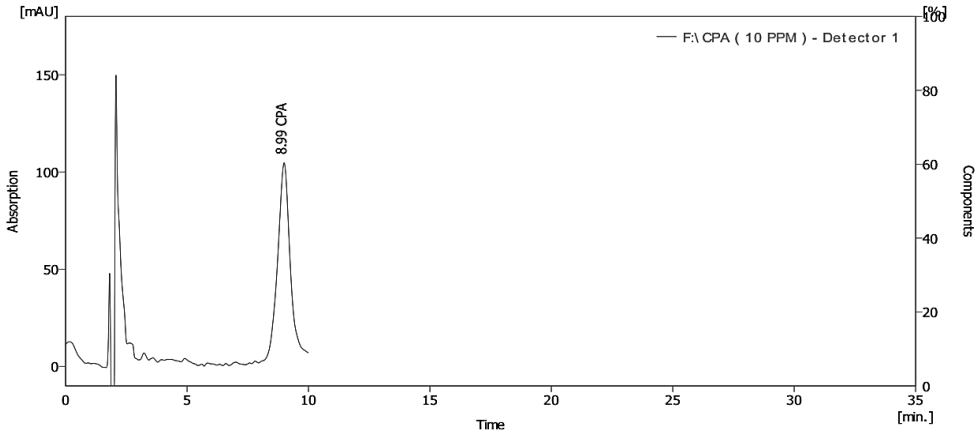

Fig. 2: Chromatogram for chloramphenicol analysis 10 ppm.

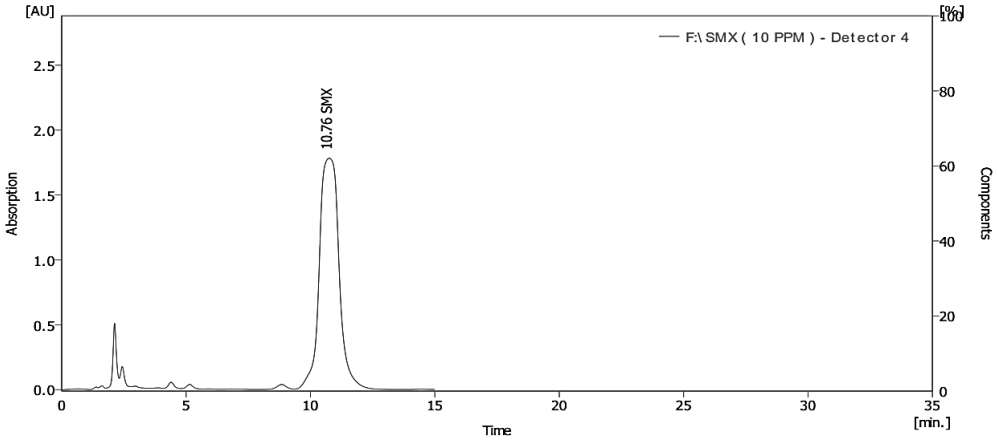

Fig. 3: Chromatogram for sulphamethoxazole analysis 10 ppm

- Preparation of synthetic sulfanilamide drug sample.
  To prepare 1000 ppm solution of the synthetic drug, 100 mg was dissolved in 50 mL of methanol. The solution was then diluted with methanol in a 100 mL volumetric flask and filtered by the same manner as used for the preparation standard drug to obtain 1000 ppm.
- To prepare synthetic solution containing mixture of 500 ppm CPA, SMX and SNA dissolved in 10 ml methanol 0.05 g of each one and then diluted with Methanol in a 100 ml volumetric flask and filtered by the same method used to prepare the standard drug.

3. Results and Discussion

3.1 Method Development

C18-ODS reverse-phase column with 250mm long and 4.6mm inner diameter (German) was used for the analysis of chloramphenicol Fig.(2), Sulphamethoxazole Fig.(3) and Sulfanilamide Fig.(4), respectively. The chloramphenicol-sulfamethoxazole and sulfanilamide were separated from each other in a mixture. Regarding the mobile phase, a mixture of 2% orthophosphoric acid solution and methanol was used.

For the development of the isolation and symmetry of the peak, the mobile phase component was changed until the best composition was chosen; Isocratic elution has been employed in this study, where a decrease in flow rate was observed from the sixth minute until the end of the analysis to obtain better results, Table (1).

0.010 mg per ml (10 ppm) standard solutions chloramphenicol sulfanilamide and sulphamethoxazole were prepared by diluting 1 mL stock standard solutions of each one to 100 mL with methanol.

To prepare a solution for a mixture of the three compounds chloramphenicol, sulfanilamide and sulphamethoxazole at a concentration of 10 ppm for each one of them, 1 ml of the stock solution of a compound is added in the same volumetric flask (100 ml), and then completed the volume to the mark with methanol.

2.4. Preparation of sample solutions.

- Chloramphenicol and sulphamethoxazole in pharmaceutical.

  10 tablet or capsules was grinded and mixed well. To prepare 1000 ppm of sample solution, an amount of the powder equivalent to about 100 mg of chloramphenicol or sulphamethoxazole was accurately weighted and 50 mL of methanol was added for chloramphenicol or 50 mL of methanol was added for sulphamethoxazole. The solution was shaken and swirled before dilution to 100 mL with methanol in a volumetric flask. The un-dissolved materials were then filtered-off using Whatman filter paper No.41, and the first portion of the filtrate was discarded, before use. More dilute solutions were prepared freshly via diluting the stock solution with methanol as required, and the proposed method was applied for the determination of chloramphenicol content or sulphamethoxazole.

2. Materials and Methods

2.1. Chemicals

Methanol HPLC, Ethanol HPLC and orthophosphoric acid are from Merck and distilled water. Chloramphenicol, Sulfanilamide and Sulphamethoxazole drugs were provided by the State Company for the Pharmaceutical Industry and Medical Devices Samara – Iraq (SDI) in pure form (99.99%).

Reagents solutions: D.W (2 % orthophosphoric acid).

2.2. Apparatus

HPLC system (Sykam HPLC system, German) with an S- 1122 Solvent delivery system, an S-5200 sample injector, S-4011 column thermos controller, and fluorescent detector (Shimadzu – Japan) used, C18-ODS reverse-phase column with 250mm long and 4.6mm inner diameter (German). The Ezchrom Elite software is used. At room temperature the column is kept.

2.3. Standard Solutions and HPLC Conditions.

A solution of 2 % orthophosphoric acid was prepared by diluting 23.5 ml 85% orthophosphoric acid with water in 1000 ml volumetric flask to the mark.

Stock standard solutions of chloramphenicol sulfanilamide and sulphamethoxazole were made by dissolving 100 mg of each in methanol (100 ml) to get three solutions 1.0 mg per mL (1000 ppm) concentration of everyone's.

chromatography- mass spectrometry (LC–MS) (Herrera, *et al.*, 2013; Wang & Zhang, 2012 and Sorayya & Parvin, 2013).

The current work aims to find and validate the method of HPLC for the determination of three bacteriostatic antimicrobial compounds chloramphenicol, Sulfanilamide and Sulphamethoxazole in pure form, synthetic mixture preparations and pharmaceutical preparations. Method validation will be included accuracy, precision, specificity, linearity and range. The method can detect and appreciate the three drugs.

Developing a simple method of RP - HPLC for the determination of Chloramphenicol, Sulphamethoxazole and sulfanilamide individual and in mixture was the objective of this work.

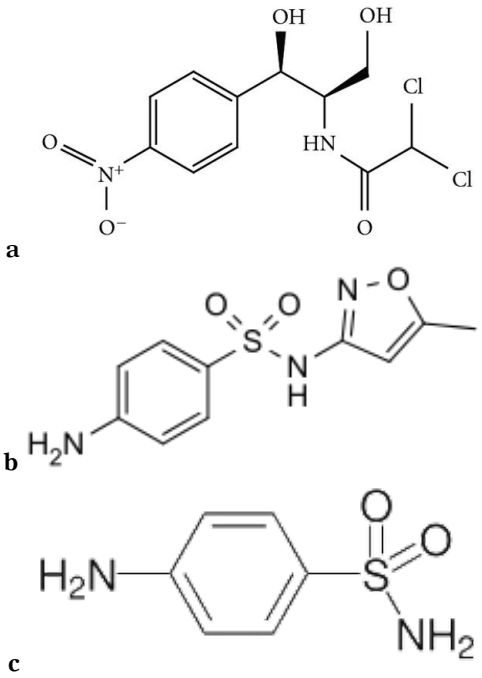

Fig. 1: (a) Structure of Chloramphenicol, (b) Sulphamethoxazole and (c) Sulfanilamide.

1. Introduction

Chloramphenicol (CPA) 2,2-dichlor-N-[(aR,bR)-b-hydroxy-a-hydroxymethyl-4-nitrophenethyl] acetamide produced by the growth of Streptomyces Venezuela or prepared synthetically_(The Pharmaceutical Codex,1979). It is an antibacterial drug helpful for the therapy of infections some bacterial (Vigh & Inczedy, 1976). It considered the first antibiotic synthesized widely. Chloramphenicol is active against broad spectrum micro-organisms. In ointment or eye drops Chloramphenicol is used to treat bacterial conjunctivitis (Vigh & Inczedy, 1976), (Fig. 1: a).

Sulphamethoxazole (SMX), Amino-N-(5-methylisoxazol-3-yl)-benzene sulfonamide is an antibiotic. It was applied to bacterial contagions such as infections of the urinary tract , bronchitis, and prostatitis and is active against both gram negative such as *E. coli & Listeria monocytogenes and positive bacteria* (Drug Bank,2015). (Fig. 1: b).

Sulfanilamide (SNA) ***p*-Amino benzene sulfonamide** is a sulfonamide antibacterial. Chemically, it is an organic compound containing aniline derivative with a sulfonamide group (Lipman,1993), (Fig.1: c).

Many methods have been used to analyze chloramphenicol in the presence of it is impurities by High-Performance Liquid (Sadana & Ghogarey,1991; Al-Rimawi and Kharoof, 2011 and Downy & Widart, 2013). HPLC methods for analysis of sulfanilamide (Sokolova & Chemyaev, 2005; Kilinc, *et al.*, 2009 and Waleed, *et al.*, 2013). Different methods of analysis have been reported for the determination of SMZ, including liquid

المستخلص

اقترحت هذه الدراسة لتحليل العقاقير الكلورامفينيكول (CPA) والسلفاميثوكسازول (SMX) والسلفانيلاميد (SNA) بطريقة كروماتوكرافيا السائلة الطور العكسي والتي تكون على شكل مستحضرات صيدلانية وخليط صناعي. بالنسبة لهذه الطريقة ، تم استخدام العمود C18-ODS (25 سم × 4.6 مم) مع مرحلة شطف متغيرة النسب للطور المتحرك الذي تتكون من الميثانول و 2٪ من حمض الفوسفوريك ، كاشف الفلورسنت (الاثارة = 310 نانومتر ، الانبعاث= 440 نانومتر). وجد أن وقت الاحتجاز او الاستبقاء لـ 0.02 ± 8.99 (CPA) و و 0.2 ± 8.21 .(SNA) و (0.2 ± 10.76 SMX) دقيقة على التوالى. تم التحقق من صحة الطريقة المقترحة من خلال قياس حدود الكشف والمعادلة الخطية والضبط والدقة. الطريقة حساسة مع حد الكشف (0.016 جزء في المليون و0.044 جزء في المليون و 0.184 جزء في المليون) لـ CPA و SMX و SNA على التوالي. دقة الطريقة 100.0٪ ودقة هذه الطريقة التي تعكسها معامل التباين (CV) للتكرارات هي (0.002 ، 0.002 و 0.0025) لكل من CPA و SMX و SNA على التوالي. لأغراض التحليل الروتيني ، يمكن لهذه الطريقة مراقبة العقاقير في المستحضرات الصيدلانية التي يتم تناولها.

الكلمات المفتاحية: كروماتوغرافيا السائلة عالية الاداء ، كلورامفينيكول ، سلفاميثوكسازول ، سلفانيلاميد.

Abstract

This study proposed to analyze chloramphenicol (CPA), sulfamethoxazole (SMX) and sulfanilamide (SNA) drugs by reverse phase liquid chromatography method in the form of pharmaceutical preparations and synthetic mixture. For this method, column C18-ODS (25 cm × 4.6 mm) was used with an isocratic elution mobile phase composed of methanol and 2 % orthophosphoric acid, fluorescent detector (Ex= 310 nm, Em= 440 nm). It was found that the time of retention for CPA, SMX, and SNA 8.99 ± 0.02, 10.76 ± 0.2, and 8.21 ± 0.2 min. respectively. The suggested method has been validated for limit of detection, limit of quantitation, linearity, Accuracy and Precision. The method is sensitive with a detection limit (0.016 ppm, 0.044 ppm and 0.184 ppm) for CPA, SMX, and SNA respectively. The method accuracy 100.0% and the precision of this method that reflects by Coefficient of variation (CV) for the repeats is (0.002, 0.002 and 0.0025) for CPA, SMX, and SNA respectively. For routine analysis purposes, this method can monitor the drugs in the ingested pharmaceutical preparations.

Keywords: HPLC, Chloramphenicol, Sulphamethoxazole, Sulfanilamide.

Analysis of Chloramphenicol, Sulphamethoxazole and Sulfanilamide Drugs by Reversed- Phase High- Performance Liquid Chromatography with Fluorescent Detector

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تحليل عقاقير الكلورامفينيكول، سلفاميثوكسازول والسلفوناميد بطريقة كروماتوكرافيا السائلة الطور العكسي عالية الأداء مع كاشف الفلورسنت

م. د. طارق ياسين محمود، م. د. عزيز لطيف جار الله و م. م. عصام شاكر حمزة

قسم تقنيات المختبرات المرضية، كلية الاسراء الجامعة – بغداد \ العراق

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Another hypothesis (electromagnetic field) indicates that the electromagnetic field is exponential, and this was followed by other hypotheses that try to explain the adaptation of genes of *Homo sapiens* comparing with adaptation of genes from other mammals during evolution.

One of the main obstacles is that (Gene regulatory elements) are often a few nucleotides long, which prevent them for calculating and estimating (the acceleration rate) from a statistical point of view.

Researchers suggest that during life-threating accidents, the brain, in order to remember previous experiences, will double-strand break (DSB) the DNA inside neurons to induce rapid gene expression. Those genes produced new connections with cells through synapses, a phenomenon known as (Synaptic plasticity) which plays an important role in learning and saving long and short memories, but more researches are needed to explore the different aspects of synaptic plasticity.

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a mysterious process (not discovered yet), so memories (usually a way of doing things, not a memory of what happened) can possibly be passed to the next generation. This could explain why children of people in a certain profession are will follow their parents in that profession (Navarro *et al*, 2004, Messing, 2020).

The funny thing is that even when a person has no idea how his/her brain is working? That person accepts and operates according to them regardless and the original question is still asked: What is thought? How do we know we have thoughts? How thoughts and emotions related? And which came first?

Many researches have to be done and will done to answer that question.

Conclusion

DNA inside neuron was arrested in G1 phase of the cell cycle which explains the absence of replication since DNA replication occurs during S phase which is preceded by G1 phase.

Environmental factors can influence the DNA code were tried in both plants and animals kingdoms in last two centuries with great success leading to the belief that environmental factors can force the brain to send signals (neurotransmitters) to somatic cells.

There are many hypotheses are trying to explain the relationship between the function of the brain and the function of DNA.

One hypothesis was assumed that all (changes of DNA expression) occur via a synaptic junction that means that the degree of on (excitatory) versus off (inhibitory) signals determines whether the neuron will be excited to release its neurotransmitter or be inhibited and inactive.

Some researchers suggest that during life-threating accidents, the brain, in order to remember previous experiences, will double-strand break (DSB) the DNA inside neurons in order to induce rapid gene expression (Bellesi *et al*, 2006).

In order to investigate the full DSB activity, researchers gave mice little electrical zaps to the feet when they entered a box to condition their (fear memory). Several methods were tried after that to assess DSBs and gene expression in the brains of the mice in the next 30 minutes in areas of the brain responsible mainly for producing, sorting and storing conditioned fear memories. All results were compared with (the control group) consists of mice did not experience the foot shock (Suberbielle *et al*, 2013; Madabhushi *et al*, 2015).

The numbers of DSBs were doubled in neurons with the formation of a (fear memory) which affect about 200-300 genes in (fear memory)'s areas (Stott *et al*, 2021).

It seems that those genes produced new connections with cells through synapses, this phenomenon is known as (Synaptic plasticity) which can be defined as (the ability of synapses to increase or decrease their activities leading to strengthen or weakness of their connections)(Abbott and Nelson, 2000; Gerrow and Triller, 2010).

Synaptic plasticity plays an important role in neurochemical foundation of learning and saving long and short memories. More research is needed to solve different aspects of synaptic plasticity and the requirement of DSBs (Abbott and Nelson, 2000; Desai *et al*, 2002; Stott *et al*, 2021).

Some researchers believe that some mother's memories (if used so often) can transfer to the mitochondrial DNA (in mother's neurons) through

Evolutionary comparisons were performed between human, chimpanzee and gorilla. One of the main obstacle that face researchers is that (Gene regulatory elements) are often a few nucleotides long, which prevent them for calculating and estimating (the acceleration rate) from a statistical point of view (Liu and Robinson-Rechavi, 2020).

DNA and memory

Every common person knows that genes instructed cells to build proteins and those proteins will regulate all functions (directly or indirectly) of the body.

A small number of genes (about 0.1% of the total) are different between people which make persons do not resemble each other. Individually, each person differ in his/her capacity of learning, memorizing or thinking, known as (cognitive function).

Cognitive function cannot be inherited (such as the color of the eye or other physical characteristics which are passed down from parents to their offspring.

That means genes cannot affect cognitive function; or can they?

The size of the brain in a human being makes it impossible for any person to keep all his/her memories from childhood to old age.

Environmental factors (such as the experiences of life, ways of education, health, emotions and others) contribute of 75% of loss of memory, while 25% of loss is contributed to genes.

Groups of researchers all over the globe are trying to identify genes which are responsible for thinking and learning, but so far only a small number have been identified. APOE, PSEN1, PSEN2 and TERM 2 are four non-inherited genes were found.

To go further with the question, a wide electromagnetic field will follow (The inverse square law) stated that (any specified physical quantity is inversely proportional to the square of the distance from the source of that physical quantity), and that means the electromagnetic field is exponential (Voudoukis, 2017).

This lead to evolve of a new therapy that practiced at present in US and many European countries known as (Transcranial magnetic stimulation (TMS)) that will relieve depression by applying magnetic pulses to the brain and seems to work for some people since their thoughts become clearer. There is a lot of debate on how this treatment works. (Groppa, 2012; Rossi, 2021), so the question remains without answers, if electromagnetic field produces electric current, so who produce the electromagnetic field. Who knows?

Evolution and brain

The brain in *Homo sapiens* differs by only 1 percent from the brain of chimpanzee in protein-coding genomes. A new hypothesis tries to explain how genes of *Homo sapiens* adapted, regulated and went through specific changes during evolution. This hypothesis claimed that the regulation of genes (gene expression) play a key role that separate (*Homo sapiens*) from other mammals which means the presence of "gene activators and gene dimmers", and not their gene sequence (Schibler, 2007).

The researchers create advanced techniques that will able them to recognize and identify vast number sets of gene regulatory regions in the brain. They use both computer models and experimental data in order to pinpoint proteins (involved in gene regulation).

axon and has a receptor that recognizes the signal from the other neuron. When the neurotransmitter is recognized it, that leads to the propagation of the signal to further neurons. (Giachello *et al*, 2016; Hosseini, 2021)

While it might be easier to think about this like a switch (all-or-nothing), most of the time it is like a dimmer switch. This means that the degree of on (excitatory) versus off (inhibitory) signals determines whether the neuron will be excited to release its neurotransmitter or be inhibited and inactive.

Thoughts and electricity

The phrase "Thoughts should be more than electric currents" is correct somehow since no one is sure what (the biological electric currents) are, or how they operate at the molecular level. Even, no one is sure why they exist or evolve in that way.

In the past, the nervous system (as a whole) was envisioned more as a plumbing system, a system containing pumps and valves with pressure to control the flow of electricity, but in the computer age, the nervous system is seen more like electrical circuitry. (Bullmore, 2004; Sidiropoulou *et al*, 2006)

Many researchers hypothesized that the neurons of most of mammals (including humans) creates an electromagnetic field extended and enclosed the brain that will transfer information to another brain (belonging to another person) and inducing consciousness, knowledge and feelings. The magnetic particles (magnetites) may play significant role in silent communication between individuals (Bullmore *et al*, 2004).

The electromagnetism theory considers the memory a kind of like a USB flash drive. Under this scenario, the electric currents play an important role (Jirsa and Haken, 1996; Tetsuo *et al*, 2016).

Cryptochromes (Crygenesfamily)arefoundin plants and animals which are involved in the circadian rhythms (Öztürk, 2008).

NOTCH2NL gene which is coded for a family of three proteins (NOTCH2NLA, NOTCH2NLB, and NOTCH2NLC) in humans which seems to play some kind of role in the growth of brain-cortex (*Fiddes et al, 2018; Suzuki et al*, 2018)

Researches in the past decades prove that nothing can change the sequence of the DNA, but (the experiences of life) can cause the occurrence of methylation (Methyl groups' attachment) to some nucleotide bases which can switch on/off the DNA expression in neurons.

That means, epigenetic changes the DNA expression of neurons which will change the way that brain operates, so, the question isn't exactly 'How does the brain affect the person's DNA?', but '**How do experiences of life affect the DNA in person's brain, and how does this affect the psychology of that person and behavior**?

Even if someone accept that neurons are responsible for changes in DNA expression, no one at present has any evidence (or even a clue) how changes in DNA expression could be achieved.

One can assume (correctly or not) that changes could be (frequency coded), (pattern coded) or just specially (coded by interconnections). None of these make sense in a noisy environment that the cells are and not really answer the question either.

One hypothesis was assumed that all (changes of DNA expression) occur via a synaptic junction. One nerve cell through axon releases a neurotransmitter into the intercellular space of the synapse. The other cell has a dendrite that is positioned exceedingly close to the other neuron's

The problem is that (Thinking and reasoning) may not be byproducts since all the above experiments do not answer the following question:

"**Is the power of thinking and reasoning and the powers of sight, hearing and so on are found in the code of DNA or are they byproducts produced by the functions of the neurons of the brain**?

Since DNA in neurons cannot replicate, so process such as (replication, transcription and translation) seems to play any role on the function of the neurons. Actually replication inside mature neurons can lead to tumors and the apoptosis of the neurons (Yang *et al*, 2001; Yang and Herrup, 2007; Frade and Ovejero-Benito, 2015).

The control of the brain over DNA is more complicated since (the electric-chemical activities of neurons) in the body represent only a minuscule fraction of the electric activity inside the brain itself.

The emergence of biotechnology and nano-biotechnology contribute advanced studies to the physiology and behavior of mammals (and other vertebrates) which have been studied for many decades, but the progress and development of technological-advanced genetic and molecular devices and the presence of advanced programming such as Gene expression programming (GEP) and Multi expression programming (MEP), for example, both are evolutionary algorithms that creates computer models to study genes help so much (Ferreira, 2001).

'**Epigenetics**' is a new area of research studies the effect of (the experiences of life) on DNA such as stress, using of drugs and so on. Therefore, many genes responsible for various behaviors were identified, isolated, and studied inside the brain. Among them:

In humans, the smoking habit will influence at least 30,000 somatic mutations in order to keep the body alive. For example, smoking increases the number of erythrocytes in blood stream by third in order for oxidative phosphorylation will be steady (Bibi *et al*, 2016; Mairi, 2013).

In general, many researchers believe that environmental factors will force the the central nervous system to send signals (neurotransmitters) from its neurons to somatic cells so they may lead change the expression of some DNA inside them (rarely that affect the genetic cells) in order to protect the body of the individual.

The neurotransmitters may lead cells to release hormones that can affect DNA expression in cells throughout the body. Actually, gene expression changes all the time; it's just part of normal cellular function (Singh *et al*, 2018; Hollander *et al*, 2020).

So, the above experiments can indicate that the nervous system can influence the code of DNA in all (or most of) the cells of the body.

Thinking and reasoning

The most important cells in the brain are found in the (region of long memory) and in the (region of short memory). A human being is capable of thinking and reasoning due the experience gained through these two regions in particular.

So, thinking and reasoning may be byproducts produced by the cells of the central nervous system (or brain in particular) since the function of these cells originates and controlled by the DNA found in the nucleus of each neuron cell (Bassett *et al*, 2006; Achard *et al*, 2008).

This led to many high-level debates about “nature vs. nurture”.

Today, many scientists believe that the only natural instinct remain in human is the sucking of milk by the baby from his mother’ breasts. All other behaviors in humans are taught through traditions, culture, and customs of the society (Zaky, 2015).

Experiments to show that influence of environmental factors can influence the DNA code were tried in both plants and animals kingdoms in last two centuries, for example; The seeds of a single wild mustard plant (*Brassica juncea*) were divided into groups and planted in a certain mountain slope but at different altitudes, with different conditions such as (different soil pH, different amount of rainfall/water, a different number of hours of sunlight, different average temperature, and different concentrations of minerals in the soil).

The seeds, though they all came from the exact same parent plants, they grow into very different types of plants with different appearances that they may not even seem to be the same species. Yet, they came from the very same seed. However, if they had been planted at the same altitude, in the same soil, with the same pH, exposed to the same number of hours of sunlight, and the same amount of rainfall, they would look nearly identical.

From the seeds of a wild single mustard plant, at least 5 different types of plants: Broccoli, Brussel sprouts, kale, cabbage and Kohlrabi are obtained (Nawaz *et al,* 2018; Raekim *et al*, 2010; Sunil and Swaroop, 2020).

Identical twin monozygotic dogs raised in different parts of the world, given different diets, different exercise/play routines, and different types of training will have different behaviors and become two completely different dogs (Aldosari *et al*, 2020).

apoptotic of neurons in cases of several diseases such as long-term smoking and Alzheimer (Anazawa *et al* 2004; Frade and Ovejero-Benito, 2015).

Actually, this is the reason, also, why neurons are no affected by x-ray or radioactivity since their DNA cannot be mutated (except in case of heavy doses of radiation).

Environmental factors and DNA

A question is asked always (Are the genes control the brain? or is the brain controls the genes?)

The brain has no effect on the genetic structure of any DNA inside a cell, but this matter is more complicated than one can think about it.

In the past, many scientists believed that all human behaviors were genetically determined. People were wondering if they can have “football genes”, “art genes” or even "leadership genes".

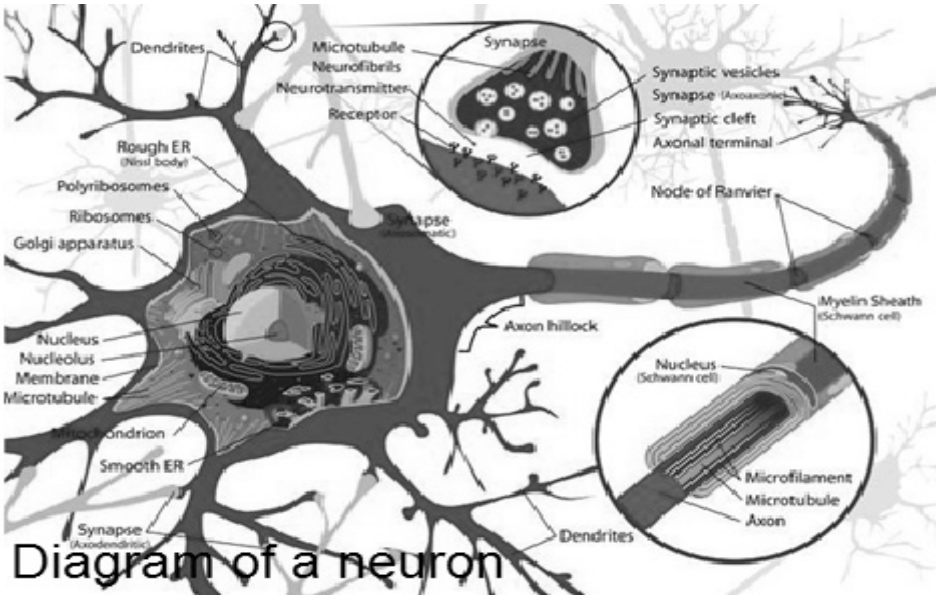

Fig.1. A neuron

Introduction

The nervous system consists of approximately 86 billion nerve cells (or neurons). The neurons are not limited to the brain, but distribute throughout the body forming the central nervous system (CNS) as well as the peripheral nervous system (PNS).

A neuron can be defined as electrically excitable cell. It consists of a soma (the body of the cell containing nucleus and organelles), a single axon (which is long and slender covered by fatty substances (myelin) to insulate it) and very short dendrites (Day *et al*, 2005; Petralia *et al*, 2015).

The function of a neuron is to produce Neurotransmitters (containing information) that travel from axon into dendrites through synapses (an intracellular space between the two neurons in order to communicate). Neurotransmitters are electric, chemicals or electric-chemicals that are released by neurons through its axon in a synapse (Debanne, 2004; Day *et al*, 2005).

Axons differ from dendrites by several features, such as shape and length (dendrites are short with many ramifications while axons are long, tail-like with less ramifications), location (dendrites are found in neurons and all cells of the body while axons are found in neurons only) and function (dendrites receive neurotransmitters whereas axons transmit them) (Petralia *et al*, 2015)

Examples of a neurotransmitter: Dopamine, acetylcholineamine

Each neuron has a DNA molecule (inside the nucleus) that does not replicate since it arrests in G1 phase of the cell cycle which explains the absence of replication since DNA replication occurs during S phase which is preceded by G1 phase, so the DNA cannot replicate in neurons.

A variety of mechanisms controls G1/S regulation and influenced by environmental factors and the neuronal phenotype itself which can leads to

مقابل الأشارات المثبطة، بينما تشير فرضية المجال الكهرومغناطيسي (قانون التربيع العكسي) إلى أن المجال الكهرومغناطيسي أسي (exponential)، بينما تحاول فرضيات أخرى تفسير تكيف جينات الإنسان العاقل مقارنة بتكيف الجينات من الثدييات الأخرى أثناء عملية التطور، حيث ذكرت هذه الفرضية أن تنظيم الجينات (التعبير الجيني) وليس التسلسل الجيني يلعب دورًا رئيسيًا يفصل (الإنسان العاقل) عن الثدييات الأخرى، مما يعني اهمية وجود "منشطات ومثبطات الجينات".

إحدى العقبات الرئيسية هي أن (العناصر التنظيمية للجينات) غالبًا ما تكون طويلة من النيوكليوتيدات، مما يمنعها من حساب وتقدير (معدل التسارع) من وجهة نظر إحصائية.

اشارت بعض الأبحاث الى أنه أثناء الحوادث التي تهدد الحياة، فإن الدماغ، من أجل تذكر التجارب السابقة، سوف يكسر (DSB) الحمض النووي داخل الخلايا العصبية للحث على التعبير الجيني السريع. أنتجت هذه الجينات روابط جديدة مع الخلايا من خلال المشابك، وهي ظاهرة تُعرف باسم (Synaptic plasticity) والتي تلعب دورًا مهمًا في التعلم وحفظ الذكريات الطويلة والقصيرة، ولكن هناك حاجة إلى مزيد من الأبحاث لاستكشاف الجوانب المختلفة بذلك.

الكلمات المفتاحية: Electric current, Neurons, Gene expression, Synapsis, Thoughts

One of the main obstacles is that (Gene regulatory elements) are often a few nucleotides long, which prevent them for calculating and estimating (the acceleration rate) from a statistical point of view.

Researchers suggest that during life-threating accidents, the brain, in order to remember previous experiences, will double-strand break (DSB) the DNA inside neurons to induce rapid gene expression. Those genes produced new connections with cells through synapses, a phenomenon known as (Synaptic plasticity) which plays an important role in learning and saving long and short memories, but more researches are needed to explore the different aspects of synaptic plasticity.

Keywords: Electric current, Neurons, Gene expression, Synapsis, Thoughts.

المستخلص

تنتقل الناقلات العصبية عبر المشابك التي تطلقها الخلايا العصبية، ولا يتكاثر الحمض النووي داخل الخلايا العصبية لتوقف المرحلة G1 من دورة الخلية وهو ما يفسر عدم وجود انقسام لعدم وجود المرحلة S التي تسبقها المرحلة G1، وأظهرت تجارب على كائنات حية (نباتية او حيوانية) خلال القرنين الماضيين امكانية تأثير العوامل البيئية على الشفرة الوراثية للحمض النووي، مما أدى إلى الاعتقاد بأمكانية سيطرة العوامل البيئية (بصورة او باخرى) على الجهاز العصبي واجباره على إرسال إشارات إلى الخلايا الجسدية.

السؤال التالي سيكون "هل قوة التفكير والتفكير موجودة في الشفرة الوراثية للحمض النووي أم أنها منتجات ثانوية تنتجها وظائف الخلايا العصبية؟

تُظهر تقنيات التكنولوجيا الحيوية والتكنولوجيا الحيوية النانوية أن (تجارب الحياة) يمكنها تشغيل/إيقاف تعبير الحمض النووي في الخلايا العصبية مما يؤدي إلى تغيير الطريقة التي يعمل بها الدماغ.

تحدث جميع (التغييرات في تعبير الحمض النووي) عبر مفترق متشابك (في إحدى الفرضيات) مما يعني تحفيز او تثبيط الناقل العصبي اعتماداً على درجة الإشارات المحفزة

Abstract

Neurotransmitters travel through synapses released by neurons. The DNA inside the neurons does not replicate since it arrests in G1 phase of the cell cycle which explains the absence of replication since DNA replication occurs during S phase which is preceded by G1 phase.

Experiments show that environmental factors can influence the DNA code were tried in both plants and animals kingdoms in last two centuries with great success leading to the belief that environmental factors can force the brain to send signals (neurotransmitters) to somatic cells.

The next question will be "**Is the power of thinking and reasoning are found in the code of DNA or are they are byproducts produced by the functions of the neurons**?

Biotechnology and nano-biotechnology techniques show that (the experiences of life) can switch on/off the DNA expression in neurons which lead to change the way that brain operates.

One hypothesis was assumed that all (changes of DNA expression) occur via a synaptic junction that means that the degree of on (excitatory) versus off (inhibitory) signals determines whether the neuron will be excited to release its neurotransmitter or be inhibited and inactive.

An (electromagnetic field) hypothesis follow (The inverse square law) indicate that the electromagnetic field is exponential, and this was followed by other hypotheses that try to explain the adaptation of genes of *Homo sapiens* comparing with adaptation of genes from other mammals during evolution. This hypothesis claimed that the regulation of genes (gene expression) play a key role that separate (*Homo sapiens*) from other mammals which means the presence of "gene activators and gene dimmers", and not (their gene sequence).

The Relationship between the Nervous System and DNA Expression (A Review)

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numerous researchers also reported higher level of anti-CdtB in IBS patients when compared with healthy controls (Pimentel *et al.,* 2015; Rezaie *et al.,* 2017; Talley *et al.,* 2019; Zaki *et al.,* 2021). Moreover, the present results demonstrated a considerable rise in serum this is in agreement with Cenac *et al.* (2007) who observed that the release of histamine and the tryptase enzyme are already increased in IBS due to activation of mast cells. While Buhner *et al.* (2009) indicated increased histamine levels at disease sites such as IBD and IBS are still not understood.

In concerning with its correlation with other biomarkers, the current study found that the serum level of histamine is increased with increasing anti-CdtB level (Table-2). This result may indicate that anti-CdtB play a crucial role in stimulating degranulation process in basophil and mast cells. Previous studies reported that microbial dysbiosis within the gut has been implicated in intestinal barrier dysfunction, visceral hypersensitivity, impaired gastrointestinal motility, and altered immune response. Therefore, the gut microbiota has emerged as a potential factor that contributes to the pathophysiology of IBS (Quigley, 2018; Mari *et al.,* 2020). Moreover, various studies have consistently shown the efficacy of microbiota-directed therapies and dietary changes in alleviating IBS symptoms (Herndon *et al.,* 2020). Recently, it has been thought that antibiotics seem to contribute to all aspects of IBS pathogenesis because they act as a major disruptor of the gut microbiota (Mamieva *et al.,* 2022).

Discussion

Since the majority of IBS patients in the present study are females (F/M ratio= 2.23), the most subtype of IBS recorded is constipation subtype (Table-1). This finding is comparable with those obtained by other studies which indicated that IBS predominantly affects women at a ratio of 2:1, with female patients presenting with more constipation and abdominal pain, rather than diarrhea (Harris *et al.,* 2016; Flanagan and Spangler, 2021).

Concerning with biomarkers, the present results indicated a high level of IL-1β in serum of IBS patients compared to healthy controls as shown in Figure-1, which is in agreement with Güven *et al.* (2022), who found a substantial rise in the rate of IL-1β in IBS patients. It is well understood that IL-1β is a powerful pro-inflammatory cytokine that is essential for host-defense responses to infection and injury (Dinarello, 1996). According to some research, IBS patients had higher blood cytokine levels (Dinan *et al.,* 2006). Also, the production of cytokines from peripheral blood mononuclear cells (PBMCs) from the blood frequently reflects the severity of inflammation, particularly IL-1β, which is thought to reflect disease activity because peripheral immune cells interact with intestinal epithelial cells and cytokines released by PBMCs to modulate intestinal barrier function. As a result, impaired mucosal barrier function may be related to PBMC-mediated cytokine release, implying a role for immunological activation in a subset of IBS patients (Holtkamp *et al.,* 1995; Liebregts *et al.,* 2007).

According to anti-CdtB, the present result demonstrated a high serum level of Anti-CdtB in IBS patients compared to healthy peoples. This biomarker is recognized to play a significant impact on the development of IBS symptoms (Smith and Bayes, 2006). In agreement with present results,

However, the correlations between histamine and IL-1β (r= 0.251, P= 0.108) as well as between anti-CdtB and IL-1β (r= 0.096, P= 0.545) are non -significant as shown in Figure-5 and Figure-6 respectively.

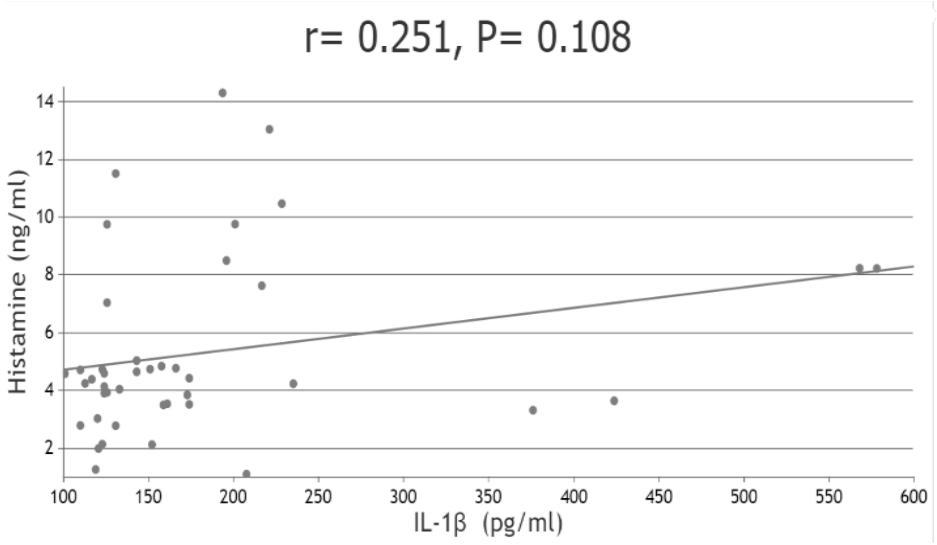

Figure-5: Correlation of IL-1β level in serum of IBS patients with their histamine

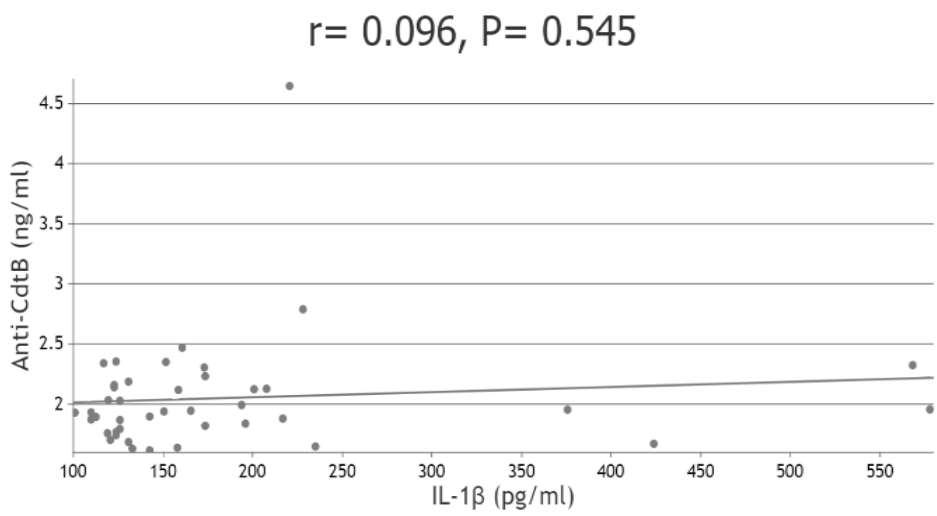

Figure-6: Correlation of IL-1β level in serum of IBS patients with their anti-CdtB

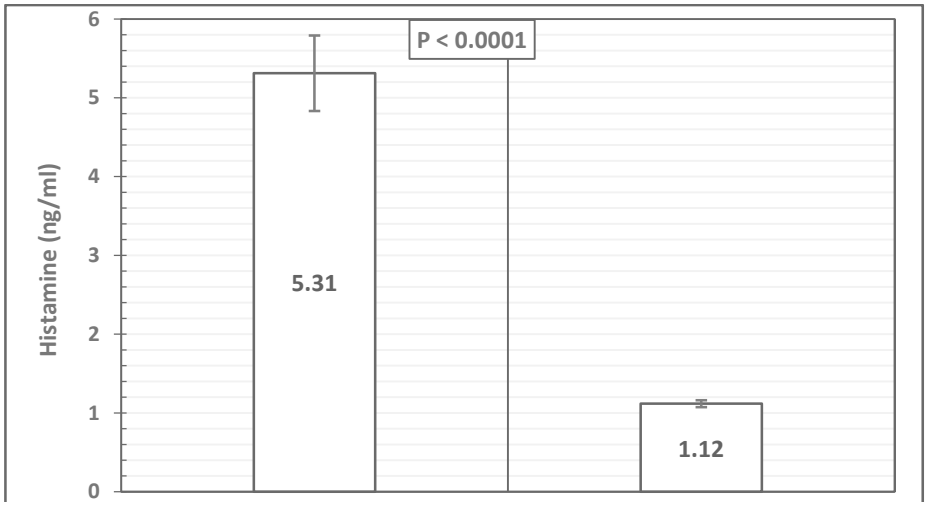

Figure-3: Serum level of histamine in IBS patients and control groups

On the other hand, Pearson's correlation calculator shows significant positive correlation between histamine level in serum of IBS patients and their anti-CdtB level (r= 0.430, P= 0.004) (Figure-4).

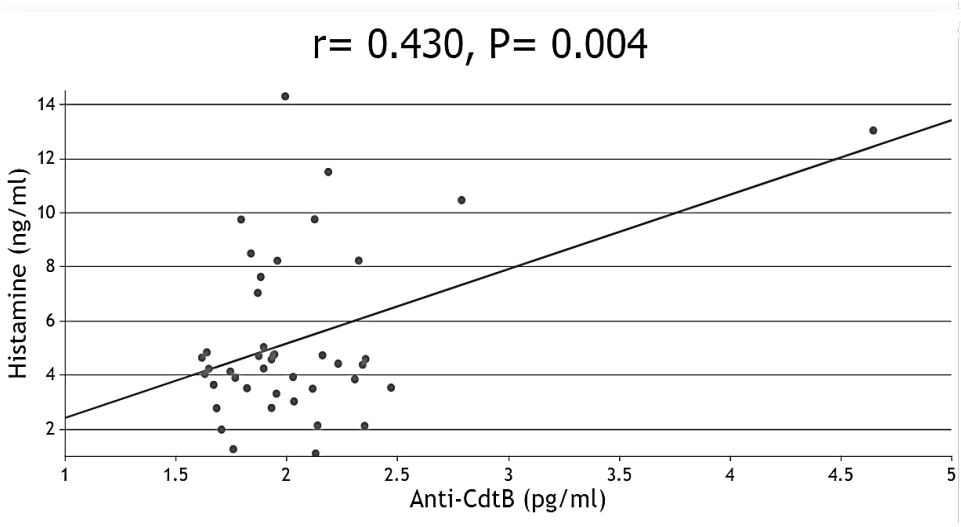

Figure-4: Correlation of anti-CdtB level in serum of IBS patients with their histamine

which are significantly higher than those in control group (85.5 ± 3.3 pg/ml, 1.4 ± 0.02 ng/ml, and 1.12 ± 0.04 ng/ml respectively) as shown in Figure-1, 2, and 3.

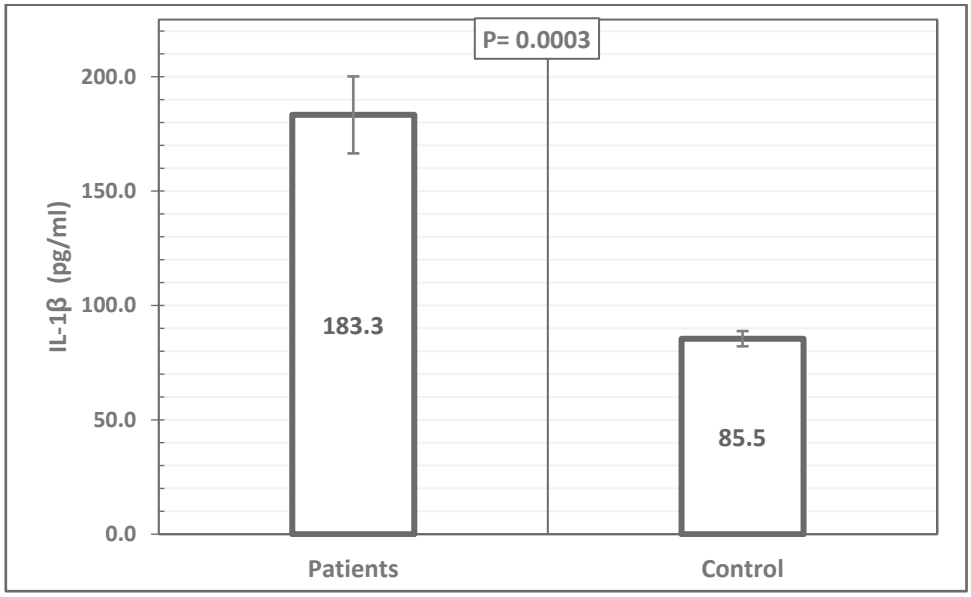

Figure-1: Serum level of IL-1β in IBS patients and control groups

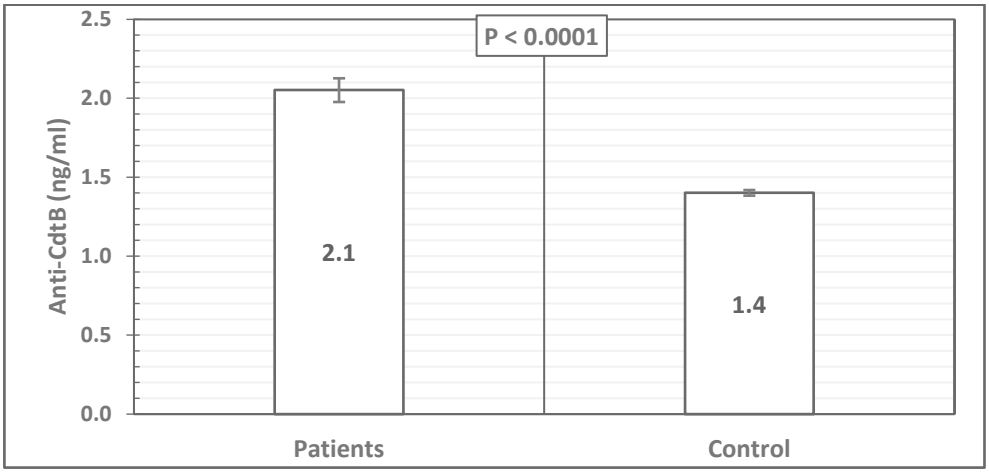

Figure-2: Serum level of anti-CdtB in IBS patients and control groups

and difference between two groups is performed by Chi square test. Pearson's correlation calculator test examines the relationship between two variables. Any difference at the P level less than 0.05 are regarded as significant.

Results

Results in Table-1 shows that the most frequent subtypes of IBS is constipation subtype which constitutes about 69% of total patients, while those with IBS-d and IBS-m constitute about 16.7% and 14.3% respectively. Also, this table reveals non-significant difference in the age and gender between patients and control groups. However, the age of patients at disease onset is 27.8 ± 12.5 year, and females are more affected with IBS in a female/ male ratio (F/M) about 2.23.

Table-1: Subtypes of IBS patients and their age and gender in corresponding with control group

Medical history		Patients (n=42)	Control (n=20)	P value
IBS subtype (n, %)	IBS-c	29 (69%)		
	IBS-d	7 (16.7%)		
	IBS-m	6 (14.3%)		
Age (year) (M ± SD)	Current	32.5 ± 12.1	33 ± 10.2	0.888
	At disease onset	27.8 ± 12.5		
	Disease duration	5.2 ± 3.3		
Gender (n, %)	Female	29 (69%)	12 (60%)	0.481
	Male	13 (31%)	8 (40%)	
	Female: Male ratio	2.23: 1		

In concerning with IBS-related biomarkers, the M ± SE of serum levels for all biomarkers (IL-1β, anti-CdtB, and histamine) in patients are equal to 183.3 ± 16.8 pg/ml, 2.1 ± 0.07 ng/ml, and 5.31 ± 0.48 ng/ml respectively,

necrosis factor-α (TNF-α) and lower levels of anti-inflammatory IL-10 in both serum and the intestinal mucosa (Choghakhori *et al.,* 2017).

On the other hand, it has been reported that progression to IBS in a rat model was accompanied by the detection of a specific bacterial toxin named cytolethal distending toxin B (CdtB) after infection with Campylobacter jejuni (Pokkunuri *et al.,* 2012). After development of anti-CdtB, it is able to cross-react with vinculin, a host cell adhesion protein present in interstitial cells of Cajal (ICC) and the myenteric ganglia that control the normal activity of the intestinal tract (Pimentel *et al.,* 2015). This autoimmunity may profoundly affect the host immune response to infections with C. jejuni, and subsequently leading to IBS (Rezaie *et al.,* 2017). The serum levels of anti-CdtB and anti-vinculin has been detected to identify patients with IBS-D, and to differentiate it from other IBS subtypes (Morales *et al.,* 2019; Zaki *et al.,* 2021).

Materials and Methods

Case-control study was carried out on 42 Iraqi patients with IBS and 20 normal individuals who were matched in age and gender to the patients to act as the control group. Diagnosis of IBS and its subtypes is confirmed based on Rome IV criteria under supervision of specialists in gastrointestinal diseases. From all patients and normal subjects, the serum levels of biomarkers (IL1β, Anti-CdtB, and Histamine) were determined by using diagnostic kits from (BioSource, USA) for IL1β and histamine, and from (Creative Diagnostics, USA) for Anti-CdtB based on sandwich enzyme-linked immune sorbent assay technology (Sandwich ELISA) (Crowther, 1995). The difference between two independent groups was statistically evaluated by using the t-test, while categorical data were reported as percentage values,

Introduction

Irritable bowel syndrome (IBS) is a common gut disorder that affects approximately 11% of the global population (Canavan *et al.,* 2014). Depending on their bowel habits changes predominance, Rome criteria classified subjects with IBS into different sub-groups including IBS with constipation (IBS-C), IBS with diarrhea (IBS-D), Mixed IBS (IBS-M), and Un-subtyped IBS (Lacy and Patel, 2017). IBS is a common gastrointestinal disorder negatively affects the quality of life of patients and imposes a significant socioeconomic burden (Black and Ford, 2020). Although the etiology and underlying pathophysiology of IBS remain incompletely understood, visceral hypersensitivity, impaired gut motility, increased intestinal permeability, emotional disorders, and changes in the immune system are proposed mechanisms involved in its pathogenesis (Holtmann *et al.,* 2016; D'Antongiovanni *et al.,* 2020; Hadjivasilis *et al.,* 2019; Casado-Bedmar and Keita, 2020). Different biomarkers have been investigated to diagnose or classify IBS, among these biomarkers; three types of biomarkers are identified in IBS patients of the present study including; human interleukin-1 beta (IL-1β), anti-cytolethal distending toxin B (Anti-CdtB), and Histamine.

In colonic biopsies from patients with IBS, an increased number of mast cells have been found in close proximity to enteric nerve fibers and have been thought to be key players in intestinal mucosal inflammation that associated with the severity of symptoms (Enck *et al.,* 2016; Wouters *et al.,* 2016). When mast cells undergo degranulation, they release inflammatory mediators (histamine, serotonin, and proteases), resulting in lymphocyte activation and cytokine imbalance. Therefore, patients with IBS were found to have higher levels of proinflammatory interleukin (IL-6, IL-8, IL-1β), tumor

المستخلص

متلازمة تهيج القولون(IBS) هي اضطراب معوي شائع يصيب ما يقرب من 11٪ من سكان العالم ويؤثر سلبًا على نوعية حياة المرضى ويفرض عبئًا اجتماعيًا واقتصاديًا كبيرًا. أجريت الدراسة القائمة على الضبط على 42 مريضاً عراقياً يعانون من القولون العصبي والذين تم تقديمهم في عيادات خاصة لأمراض الجهاز الهضمي (GIDs)، إلى جانب 20 فردًا يتمتعون بصحة جيدة يتناسبون مع أعمارهم وجنسهم للعمل كمجموعة ضابطة. هدفت الدراسة إلى تحديد مدى تكرار الإصابة بمرض القولون العصبي لدى المرضى العراقيين، وكذلك مدى تأثير المؤشرات الحيوية على بداية المرض ونوعه وشدته مثل (IL-1β، و 'Anti-CdtB anti-Cytolethal distending toxin B'، و الهيستامين). أظهرت النتائج أن نوع الإمساك الفرعي من متلازمة القولون العصبي هو الأكثر شيوعًا بين المرضى، وتشكل الإناث غالبية مرضى القولون العصبي مع نسبة الإناث إلى الذكور حوالي 2.23: 1. حيث ان مستويات IL-1β, anti-CdtB والهستامين مرتفعه بشكل ملحوظ في مصل مرضى القولون العصبي مقارنة بمستوياتهم في المجموعة الضابطة. في مجموعة المرضى، أظهرت مضادات CdtB ارتباطًا إيجابيًا معنويًا بمستوى الهيستامين، في حين أن العلاقة بين مضادات CdtB و IL-1β وكذلك بين الهيستامين و IL-1β ليست ذات دلالة. يمكن أن نستنتج أن مضادات CdtB قد تعمل دور رئيسي في التسبب في مرض القولون العصبي بعد تعطيل ميكروبيوتا الأمعاء التي تحتاج إلى مزيد من التحقيق.

الكلمات المفتاحية: هستامين, مضاد CdtB, IL-1B و IBS

Abstract

Irritable Bowel Syndrome (IBS) is a common gut disorder that affects approximately 11% of the global population and negatively affects the quality of life of patients and imposes a significant socioeconomic burden. Control-based study was conducted on 42 Iraqi patients with IBS who were presented at private clinics for gastrointestinal diseases (GIDs), along with 20 healthy individuals matched in their age and gender to act as control group. The study aimed to determine the frequency of IBS among Iraqi patients, as well as the influence of biomarkers on disease's initiation, type and severity such as (IL-1β, anti- Cytolethal distending toxin B 'Anti-CdtB', and histamine). The results showed that constipation subtype of IBS is the most frequent among patients, and females constitute the majority of IBS patients with female: male ratio about 2.23: 1. The levels of IL-1β, anti-CdtB, and histamine are significantly elevated in the serum of IBS patients when compared to their levels in control group. In patients' group, anti-CdtB showed significant positive correlation with their level of histamine, while correlation between anti-CdtB and IL-1β as well as between histamine and IL-1β are not significant. It can be concluded that anti-CdtB may act as a key player in IBS pathogenesis after disruption gut microbiota which needs further investigation.

Keywords: IBS, IL-1β, Anti-CdtB, Histamine.

Influence of IL-1ß, Anti-CdtB and Histamine in Irritable Bowel Syndrome

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تأثير IL-1β, Anti-CdtB، والهستامين في متلازمة تهيج القولون

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"(Albrecht et al., 2011. Griffiths (2003) concluded that a low GCF flow suggests healthy tissue, whereas a high GCF flow denotes inflammatory tissues. Perhaps the most preferred sample method for GCF is filter paper strip selection, and this technique can be used to determine the concentration of different cytokines and other biomarkers in GCF (Gamonal, 2001). According to a study done by researchers' Hyaluronic acid gel has been demonstrated to have a similar effect to chlorhexidine in treating plaque-induced gingivitis in patients using fixed orthodontic appliances. It is advised that this gel be used as the initial treatment for plaque-induced gingivitis. (Albrecht *et al*., 2011) "type": "article-journal", "volume": "6"},"uris": ["http://www.mendeley.com/documents/?uuid=1ca18a45-1cc1-4e9b-bda9-a071436672a1"]}], "mendeley":{"formattedCitation":"(Albrecht et al., 2011. Also in another study that evaluates the therapeutic efficacy of 0.2% hyaluronic acid, they found that in addition to scale, a gel containing 0.2% hyaluronic acid is more effective than scaling alone for treating plaque-induced gingivitis(Jain, 2013).

Conclusion

When compared to the Chlorhexidine group, treatment for 7 days with Hyaluronic acid 1% with Chlorhexidine digluconate 0,20%gel (G2) was significantly more effective at reducing GCF volume (l) (G1). The use of gingival crevicular fluid in the diagnosis and treatment of plaque-induced gingivitis can be crucial.

Conflict of interest: None.

Groups (25/group)	Median	GCF(µl) at day 7		
		Kruskal-Willis Test		
		H-statistics	P-value	Result at PÂ0.05
G1	0.44	12.8279	0.002	S
G2	0.36			

G1 = CHX group; G2 = Hyaluronic acid 1% with Chlorhexidine digluconate 0,20% gel group; S = significant (P > 0.05).

Table 3: Effect of various treatments (pre and after) on gingival crevicular fluid (GCF, l) measurements taken at 0 time and day 7 in G1 and G2.

Groups	Medi	An	Wilcoxon Signed-Rank Test		P≤0.05
	Before (0-time)	After (day -7)	W-value*	The critical value of W	
G1	0.56	0.44	46.5	48	S
G2	0.54	0.36	35.5	67	S

G1 = CHX group, G2 = Hyaluronic acid 1% with Chlorhexidine digluconate 0,20% group, S = significant (P ≤ 0.05).

Discussion

GCF is a biological exudate, and analysing its components is a novel method for specifically identifying biomarkers with the necessary specificity. Both periodontology and orthodontics can benefit greatly from the examination of GCF as a diagnostic tool (Eden, 2017). Several researchers have hypothesized that gingivitis and periodontitis cause a rise in GCF levels (Huth *et al*, 2006). The findings of this investigation supported those of Gupta and Mansi (2012), who showed that when gingiva is extensively inflamed, both clinically and historically (Gupta & Mansi, 2012), GCF production increases significantly (Tables 1 & 2)(Albrecht *et al.*, 2011)"type":"article-journal","volume":"6"},"uris":["http://www.mendeley.com/documents/?uuid=1ca18a45-1cc1-4e9b-bda9-a071436672a1"]}], "mendeley": {"formattedCitation":

Results

In G1 and G2, the effects of the gels on gingival crevicular fluid volume (l) at 0 time (baseline measurement) and day 7 were noted. The median values of the (GCF) for each group (G1 and G2) measured at 0 time are (0.54 and 0.56), respectively, according to the data in Table 1. H-statistics = 1.0688 and P-value = 0.5896 when comparing the GCF median values between the two groups. On the other hand, the results at day 7 post-treatments (Table2) revealed that there were statistically significant (p0.05) differences between the two groups (0.44 and 0.36 in G1 and G2, respectively). (H-statistics: 12.8279; P-value: 0.002) Additionally, the results (Table 3) demonstrated that the median values in G1 and G2 were (0.54) died and (0.36) respectively from the pre-treatment (0-time) values of (0.56) and (0.44), respectively. In G1, this reduction had a W-value of 46.5 and a critical value of 48, however in G2, the W-value was 35.5 and the critical value was 67, making this reduction statistically significant (P 0.05).

Table 1: Gingival crevicular fluid (GCF) volume measurements at 0 time in G1 and G2 are compared.

Groups (25/group)	Median	GCF(µl) at 0-time		
		Kruskal-Willis Test		
		H-statistics	P-value	Result at P<0.05
G1	0.54	1.0688	0.5896	NS
G2	0.56			

G1 = CHX group, G2 = Hyaluronic acid 1% with Chlorhexidine digluconate 0,20% gel group. NS = non-significant (P > 0.05).

Table 2: Comparing the volume of gingival crevicular fluid (GCF) at day 7 as measured in G1 and G2

salivary contamination by gently airdrying the tooth surface for 10 seconds while utilizing cotton rolls to do so. After two minutes, the freshly produced crevice fluid was collected using a 2 6-mm (PS), 0.22 m pore size filter. Each (PS) was slowly introduced until there was no resistance, at which point it was left in place for 30 seconds. The four (PS) were removed after 30 seconds and moved to an Eppendorf tube, where they were immediately weighed and sealed.

Extraction of the GCF (elution and centrifugal procedure from PS):

300 µl of phosphate-buffered saline was used to incubate the four (PS) in each Eppendorf tube. Overnight at 4°C, samples were eluted (Refrigerator). At 400 g (2000 RPM) for 4 min, samples were centrifuged. Before being examined, the supernatants were kept frozen at -80°C (Schwendicke, 2017).

Determination of the GCF volume:

To calculate GCF volumes, all sites from each patient were combined. By using differential weighing, the main weight of GCF absorbed on the four PS was calculated using the formula: W2-W1 = MGCF (Emilson, 1977). M stands for Main GCF Weight (g), W2 for GCF Weight (after GCF collection), and W1 for GCF Weight (before GCF collection). The mean value per patient was then calculated by dividing the value by four. Using the formula Volume = Mass/Density, the acquired value, represented in g, was converted to volume (L) (Griffiths, 2003).

Data processing and statistical analysis

The statistical software SPSS ver. 11.5 (SPSS Inc., Chicago, USA) and the computer program by Walonick, 2010, Stat Pac Inc., were used to analyse the data. Non-parametric data analysis.(Walonick, 2010)

Samples collection:

Samples were taken from 50 patients in the morning, 2–3 hours after breakfast. All patients consented to ultrasonic scaling, and they were urged to practice proper dental hygiene. Chlorhexidine (group 1) and Hyaluronic acid 1% with Chlorhexidine digluconate 0,20% gel was administered to patients twice daily (morning and night) for one week Fig (1).

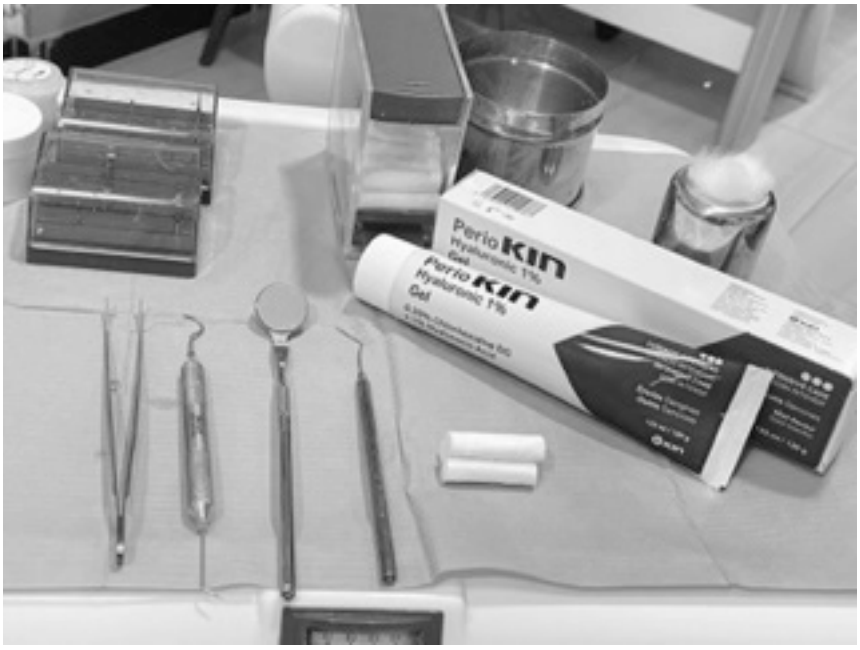

Figure (1): Application of the Hyaluronic acid 1% with Chlorhexidine digluconate 0,20% gel

Additionally, patients were instructed to wait 30 minutes following gel application before eating, drinking, or washing. Using paper strips, GCF samples were taken from each patient's four sampling tooth locations at baseline (zero-time) and day 7 (PS). Pre-secreted saliva was removed by washing the mouth cavity with water. The four incisors' four sites were then cleaned of any remaining

Materials and Methods

This research was done at a privet clinic, in Baghdad, Al-Karkh. Throughout the trial, 50 male patients with gingivitis, (25/group), were enrolled. Group 1 (G1) scaling was applied using chlorhexidine gel, while Group 2 (G2) scaling was applied using hyaluronic acid 1% with Chlorhexidine digluconate 0,20% gel.

Inclusion criteria:

- People who have mild to severe plaque-induced gingivitis.
- Ages between 18 and 30 years old
- The patients showed no signs of an actual loss of attachment.
- Willingness to provide permission.

Exclusion criteria:

- Recent use of antibiotics (within the last 3–4 weeks).
- Mouthwash usage and dental care background
- Patients who have known systemic diseases.
- 4-Smokers.

Collection of Gingival Crevicular Fluid (GCF) samples:

Four paper strips were inserted in a 1.5 mL Eppendorf tube and weighted (weight, W1) on an electronic scale before sample collection (PerioPaper Strips; Oraflow Inc., New York, USA). The primary GCF's rest calculation used the weight of the four (PS) as a reference weight. At four distinct locations on the anterior teeth, the GCF was repeatedly collected. After that, the (PS) were put into an Eppendorf tube and weighed right away.

Gingival crevicular fluid (GCF) is an inflammatory exudate that includes elements from a vascular, such as serum, connective tissue, and the epithelium through which it passes on its approach to the gingival crevice, as well as inflammatory cells and bacteria found in the tissues and crevice (Lamster & Ahlo, 2007). The GCF study is a non-invasive way to assess the pathophysiological state of the periodontium in a specific location. Wang and his colleagues (2016) highlighted the importance of GCF flow as an evaluation tool, stating that it is proportional to the degree of inflammation(Wang *et al*., 2016).

Aerobes and anaerobes of both gram-positive and gram-negative bacteria, as well as fungi-like yeasts, can be eliminated by chlorhexidine digluconate (CHX). It was initially proven to be effective in preventing plaque and gingivitis in people without practicing good dental care more than 40 years ago(Puig & Montiel, 2008). The use of chlorhexidine in several formulations for a range of oral conditions as well as its usage as an effective antibacterial agent and plaque management agent. Typically, chlorhexidine is administered as a gel or mouthwash. Chlorhexidine can be used as a paste at home or in trays in a dental office when it is in gel form. Use may occur up to three times daily for two days or once daily for ten to fourteen days. (Palwankar *et al.*, 2021).

This study aimed to detect the influence of Hyaluronic acid 1% with Chlorhexidine digluconate 0,20% gel as an adjunctive therapy on gingival crevicular fluid flow rate in patients with plaque-induced gingivitis.

Introduction

One of the most common glycosaminoglycans in the extracellular matrix is hyaluronic acid (HA), also known as hyaluronan(Amorim *et al*., 2021). Inflammatory illnesses with a long course are treated with HA. An important distinction is that periodontal disease affects the periodontium and is an inflammatory condition. Very little HA is present in the mineralized periodontal tissues of the cementum and alveolar bone, but the extracellular matrix of the gingiva and the periodontal ligament are is essential for its formation(Aydinyurt *et al*., 2020). Following HA therapy, wound healing quickens because HA receptors are affected, which affects cellular migration, angiogenesis, and inflammation. In the deeper periodontal tissues as well as the marginal gingiva, HA reduces symptoms(Abatangelo *et al*., 2020). Additionally, several periodontal treatments that involve non-surgical and surgical therapy, as well as soft and hard tissue regeneration, have made advantage of this wound-healing property of HA. Additionally, HA controls the cell-matrix and cell-cell exchanges and is essential for cell signaling, hemostasis, and these processes. The influx and outflow of nutrients and waste materials are also influenced by HA(Vigetti *et al*.,2014). The body uses HA for several functions by utilizing its physical, chemical, and biological properties. These biological activities range from fundamental structural responsibilities in the extracellular matrix to control over tissue macro- and microenvironments, effects on cell behaviour, and developmental regulation. Additionally, many HA activities have direct, receptor-mediated impacts on gene expression(Abatangelo *et al*., 2020). A reversible inflammatory condition called gingivitis can develop into periodontitis, which results in the loss of the tooth's supporting bone and soft tissue(Shrivastava *et al*., 2021).

المستخلص

الخلفية العلمية: تتطلب كل من مكونات دواعم الأسنان الصلبة واللينة حمض الهيالورونيك (HA) لكي تعمل المصفوفات خارج الخلية بشكل صحيح. HA أمر بالغ الأهمية لفهم كيفية عمل الالتهاب والتئام الجروح. تم العثور على كميات مختلفة من HA في أنسجة اللثة، بما في ذلك الأنسجة غير المعدنية مثل اللثة وأربطة اللثة، ومستويات أقل في الأنسجة المعدنية مثل الملاط والعظم السنخي. تشير الأبحاث الأولية إلى أن HA يمكن أن يتحكم في تجديد أنسجة اللثة وعلاج أمراض اللثة. في كل من أنسجة اللثة العميقة واللثة الحدية، يساعد HA في تخفيف الأعراض.

الأهداف: يهدف هذا البحث إلى الكشف عن تأثير حمض الهيالورونيك بنسبة ٪1 كعلاج مساعد على معدل تدفق السوائل اللثوية في المرضى الذين يعانون من التهاب اللثة الناجم عن البلاك.

المواد و طرائق العمل: تم تسجيل خمسين مريضاً مصاباً بـ (PIG) طوال التقرير (25 لكل مجموعة) بمتوسط عمر (18–30) سنة. تم تقسيمهم إلى مجموعتين، (G1) ازاله تكلسات وعولجت بماده الكلورهيكسيدين و (G2) ازاله تكلسات وعولجت بحمض الهيالورونيك ٪1 والكلورهيكسيدين ديجلوكونات ٪0,20 جل. لمدة أسبوع، تم توجيه المرضى لاستخدام هلام حمض الهيالورونيك لتدليك اللثة مرتين يوميًا.

النتائج: في وقت الصفر واليوم السابع، تم الحصول على GCF باستخدام شرائط ورقية (PS) من أربعة مواقع لأخذ العينات. أظهرت قيم متوسط حجم l) GCF) عند 0 ذلك من الناحية الإحصائية، بين المجموعتين. ومع ذلك، أظهرت مجموعة هلام حمض الهيالورونيك انخفاضًا كبيرًا في حجم GCF في اليوم السابع بعد العلاج. بمقارنة مجموعة هلام حمض الهيالورونيك بمجموعة الكلورهيكسيدين، أدى العلاج بالجيل الهيلارونيك إلى خفض كبير في حجم GCF (ميكرولتر)

الخلاصة: بمقارنة مجموعة حمض الهيالورونيك (G2) بمجموعة الكلورهيكسيدين، كان العلاج بحمض الهيالورونيك (G2) أكثر فاعلية بشكل ملحوظ في تقليل حجم G1) (µl) GCF).

الكلمات المفتاحية: حمض الهيالورونيك، أمراض اللثة، العلاج، السائل اللثوي المفصلي

Abstract

Background: Both hard and soft periodontal components require hyaluronic acid (HA) for extracellular matrices to function properly. HA is crucial to understanding how inflammation and wound healing work. Different amounts of HA are found in periodontal tissues, including non-mineralized tissues like gingiva and periodontal ligament, and lesser levels in mineralized tissues like cementum and alveolar bone. Preliminary research indicates that HA can control periodontal tissue regeneration and treat periodontal disease. In both deeper periodontal tissues and marginal gingiva, HA helps to relieve symptoms.

Aims: This research aimed to detect the influence of hyaluronic acid 1% gel as an adjunctive therapy on gingival crevicular fluid flow rate in patients with plaque-induced gingivitis.

Materials and methods: Throughout the study, fifty male patients with (PIG) were enrolled (25 per group) with an (18 to 30 years old) median age. They were split into two groups: (G1) scaling and receiving treatment with chlorhexidine, and (G2) scaling and receiving treatment with hyaluronic acid. 0.1 with 0.20 percent gel of chlorhexidine. For a week, patients were directed to use the Hyaluronic acid gel to massage their gingiva twice daily.

Results: At zero time and day seven, GCF was obtained using paper strips (PS) from four sampling tooth locations. The median GCF volume (µl) values at 0 time demonstrated that statistically speaking, between the two groups. The hyaluronic acid gel group, however, displayed significantly reduced GCF volume at day 7 post-treatment. Comparing the Hyaluronic acid gel group to the Chlorhexidine group, Hyaluronic acid gel treatment significantly reduced GCF volume (µl).

Conclusion: Comparing the Hyaluronic acid (G2) group to the Chlorhexidine group, the Hyaluronic acid (G2) treatment was significantly more effective at reducing GCF volume (µl) (G1).

Keywords: Hyaluronic acid, periodontal disease, treatment, gingival crevicular fluid.

Hyaluronic Acid Gel Effectiveness As An Adjunctive Treatment in Patients with Periodontal Disease

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فعالية جل حمض الهيالورونيك كعلاج إضافي في المرضى الذين يعانون من أمراض ما حول الأسنان

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4. conclusion

The industrialized RP-HPLC method offers a convenient and well-organized method for the quantitative estimation of a new modification of Vitamin B2 drug and pharmaceutical dosage form. This method has various advantages simple, precise, quick analysis time 40 days, The animal study results showed that the activity of all formulation tests to male rat all eight-male rate showed response to Vitamin B2 injection with different dose concentrations, formulation 1, 2, 3, 4 and 5) showed the ratio of area under the carve of product to the reference (35%, 56%, 108%, 144% and up to 150%) respectively and most appropriate dosage form with test formula number 4.

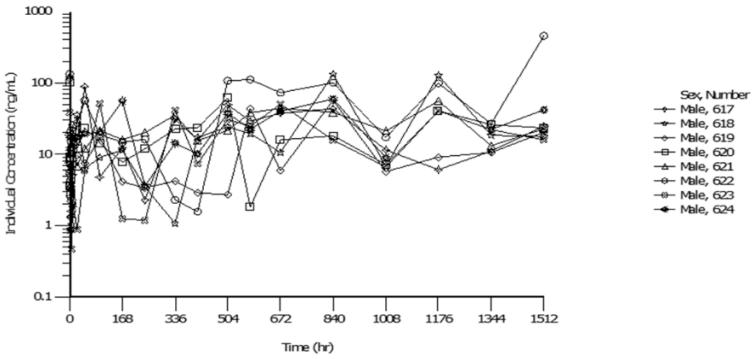


Figure (4) Individual Vitamin B2 Plasma Concentration-Time Profiles Test Formulation 3

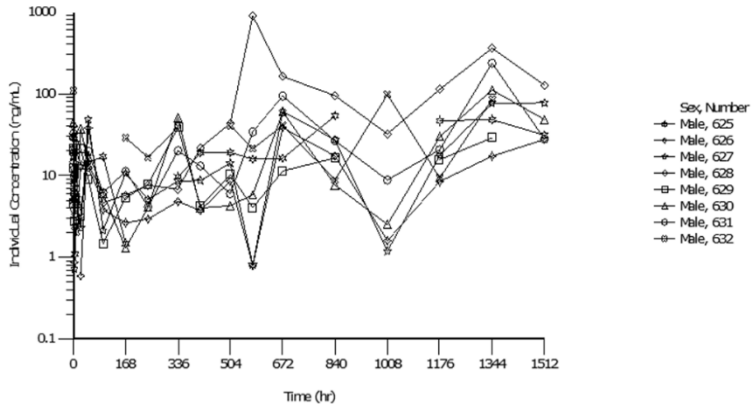


Figure (5) Individual Vitamin B2 Plasma Concentration-Time Profiles Test Formulation 4

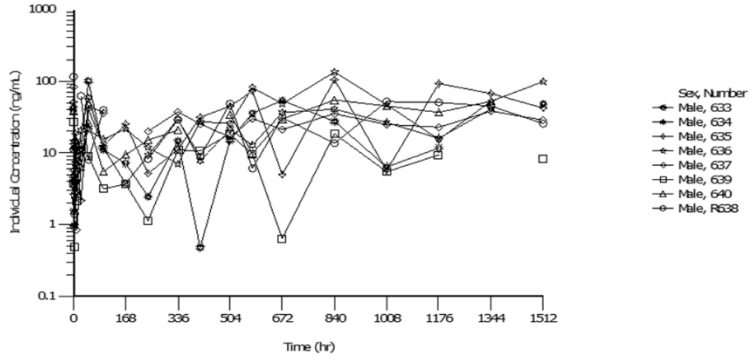
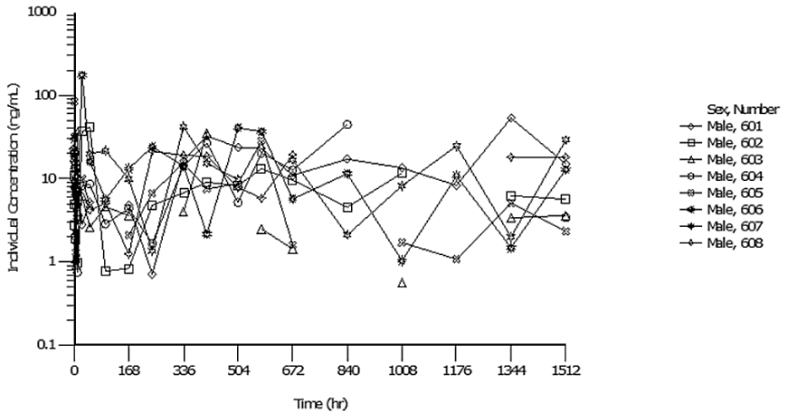


Figure (6) Individual Vitamin B2 Plasma Concentration-Time Test Formulation 5

Table(1) Bioavailability for tested formulation in rats' bioactivities

FC	F%
1	35%
2	56%
3	108%
4	144%



Figure(2) Individual Vitamin B2 Plasma Concentration-Time Profiles Formulation 1

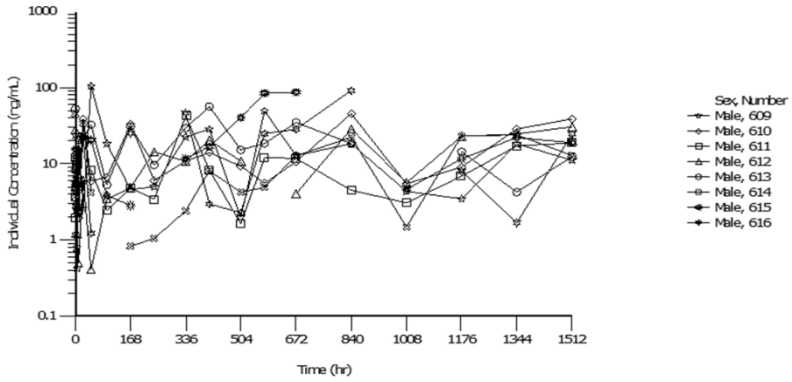
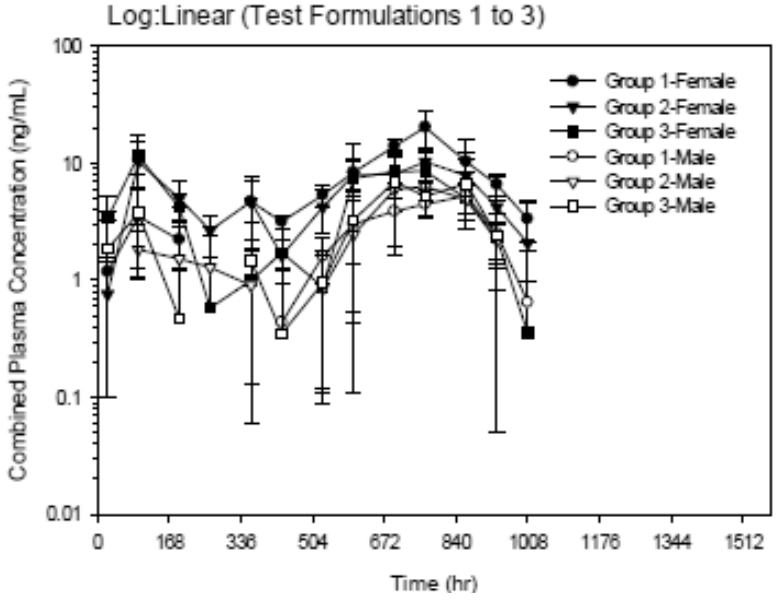


Figure (3) Individual Vitamin B2 Plasma Concentration-Time Profiles Test Formulation 2

completely released before this time point. There was no evidence of local tissue response, fibrosis, or erosion upon the micro-particles of Vitamin B2 release in the body, indicating that the micro-particles of B2 release were biocompatible locally throughout the implementation period at all-time points. All figure test formulation represents the bioavailability in different ranges.

The animal analyzing study showed five test formulations for five different patches, test of formulation patches included using eight of males and females rats with number as it is and after single subcutaneous injection of 1mg/animal of prepared vehicle of Vitamin B2 to male rats, as shown in Figure (1).



Figure(1) Individual and Mean Vitamin B2 Cmax and AUC0-1512hr Values Test Formulations or Reference Product

All figures of analyzing the animal activity for Vitamin B2 will represent in logarithmic plot. The value of bioavailability acceptable rang (80 – 125) % (Tang *et al.,* 2014), Table 1 summarized the bioavailability for all formulations patches.

3. Results and Discussion

3.1 Pharmacokinetic Studies Results

The In vivo pharmacokinetic characteristics of PLGA micro-particles were examined in rats in order to evaluate the feasibility of developing a long-term, sterile drug delivery system for Vitamin B2 supplementation. Rats were given either EO sterilized PLGA-B2 or surface sterilized (betadine wash) PLGA 50:50-B2.

The In vivo onset was quick, and the serum concentration remained within the intended range of 2-15 ng/ml for a significant amount of the release interval, despite the fact that serum levels fluctuated over time. At 14 days, serum levels were roughly 7-10 ng/ml, and by 27 and 40 days, they had climbed to approximately 15-20 ng/ml (Figures 4 - 6). As a result, the microspheres continued to supply Vitamin B2 for at least 40 days.

Following sample collection, the plasma levels for each animal were evaluated for Vitamin B2. Figures (1 to 6) represent the In vivo release over the 30-day period for each of the formulation groups. These Figures use the average plasma level of Vitamin B2 (ng/mL) for each animal at each time-point pulled.

Due to the elimination of any remaining sterile microspheres from some of the rats, the presence of Vitamin B2 was determined by HPLC/UV spectroscopy in the remaining animals. Upon analyzing the amount of drug present in the extracted samples, it is observed that the percent drug load decreases over time, indicating that the drug is being released at a faster rate than the polymer is dissolving. Approximately 25 wt. % of the micro-particles removed on day 14 have a load of approximately 1 to 1 wt. percent on day 15, 15 % on day 27, and 0 to 1 wt. % on day 30. Microspheres removed at 40 days have a drug load of about 0 wt. percent, indicating that the drug has been

2.2 Pharmacokinetic Study

The analysis was carried out using a high-performance liquid chromatography system with UV detection at 215 nm. Blood samples weighing 0.5 mL were taken at each of the three time points. The blood was centrifuged for 30 minutes, with 200 mL of serum remaining to be frozen at -80°C until analysis was performed (Fernandes *et al.,* 2007), (Elbarbry, Wilby, and Alcorn 2006) and (Niu *et al.*, 2012).

The amounts of Vitamin B2 in the serum of each animal were determined in duplicate at each of the time points. A standard solution of Vitamin B2 was prepared in normal rat serum (with a concentration range of 1.25 - 50 ng/ml). When the standard solutions were prepared, they were extracted using a process that was the same as that used for the research samples. They were included in each run to provide both the standard curve and retention time for the drug under investigation. Vitamin B2 had a retention duration of around 25 minutes when tested. It was established that the final in vivo serum concentration profile for each rat was obtained by graphing serum concentration against time for all animals (Niu *et al.,* 2012) ,(Hasimoglu and Ghodke 2018) and (Jakobsen 2008).

2.3 Behavioral Studies

Under the influence of isoflurane anesthesia, microspheres were implanted in the subcutaneous area on the dorsal surface. In order to look for indicators of initial high drug release during this period, daily qualitative evaluations of the rats being performed for five days immediately following transplantation in order to make it look for indications of increased initial drug release throughout this period.

mechanism for years (Chereddy *et al.,* 2014). In addition to medications such as antibiotics, anti-inflammatory pharmaceuticals, proteins/peptides, and nucleic acids which target different phases/signaling cycles of healing process, it is also mentioned that the cumulative therapeutic value of PLGA and a overloaded medication on injuries therapeutic are beneficial (O'Neill *et al.,* 2015).Therefore, the current study aims to optimize a fast, reproducible, reliable, and effective technique for estimating the biological activity of Vitamin B2 in injectable dose form using reversed phase high performance liquid chromatography (RP-HPLC),

2. Materials and Methods

2.1 Experimental Animals

The study's animal models were Sprague Dawley rats, both males and females, which were employed in the experiment. All protocols were approved by the University of Kentucky's Institutional Animal Care and Use Committee (IACUC), and the animals were housed in facilities recognized by the Association for Assessment and Accreditation of Laboratory Animal Care (AAALAC). The animals stayed divided into four groups of eight each for testing, with one animal left untreated as a control. The dosing technique and findings showed that the average outcomes for the four formulations were obtained, as well as their standard deviations (standard error of the mean). During the course of these investigations, a total of 28 rats were administered with loaded vitamin B2 microspheres that were implanted in the subcutaneous area on the dorsal superficial under isoflurane anesthesia, which allowed for pharmacokinetic evaluations of plasma concentration levels over time.

1. Introduction

Vitamin B2, often known as riboflavin, is one of the eight B Vitamins that are required for human health to function properly. It can be found in a variety of foods, including grains, vegetables, and dairy products (Ashoori and Saedisomeolia 2014). It is essential for the digestion of food components, the absorption of other nutrients, and the maintenance of tissues (Eussen *et al.*, 2011). B2 is a water-soluble vitamin; however, all vitamins, depending on their type, are either water- or fat-soluble (Chowdhury 1978). Individuals must consume Vitamin B2 on a regular basis since the body can store only a small amount of it and because supplies decrease quickly when not ingested (Aykroyd and Roscoe 1929), Riboflavin is found in naturally occurring forms in some foods, is added to others, and can be obtained through dietary supplements (Zylberman *et al.,* 2006)4-dihydroxy-2-butanone 4-phosphate with 5-amino-6-ribitylamino-2,4 (1H,3H. Riboflavin (Vitamin B2) is synthesized by condensing 3,4-dihydroxy- 2-butanone 4-phosphate with 5-amino - 6-ribitylamino- 2,4 (1H,3H) 6,7-dimethyl-8-ribityllumazine synthase catalyzes the formation of pyrimidinedione (lumazine synthase) (Jiang *et al.,* 2005)much progress has been made towards the clinical use of antigen-loaded microspheres. Poly(lactide-co- glycolic acids, there is two divisions of PLGA is a biodegradable polymer that has been certified as an active ingredient for parenteral administration by the Food and Drug Administration and the European Medicines Agency (Aguillón *et al.,* 2004). It is widely utilized in the pharmaceutical industry; Various medicinal applications have relied on this well-established medication delivery

Abstract

The current study aims to optimize a fast, reproducible, reliable, and effective technique for estimating the biological activity of Vitamin B2 in injectable dose form using reversed phase high performance liquid chromatography (RP-HPLC), a biodegradable polymer that has been approved as an active ingredient for parenteral administration, the vitamin loaded in PLGA (Poly (lactic-co-glycolic acid) 50:50 type, and the injection volume was 1mg of prepare. Rats, both male and female, were employed as the animals. Individually, the duration time of the hosted animal reached 40 days, and the activity of vitamin B2 was recorded in rapid hours through six weeks by HPLC device of plasma sample, the results indicate that all formulations batch response continuously through forty days, with the best one detected according to drug bioavailability with inside the permitted range, the best performance mentioned at Fabs reached 108 percent.

Keywords: Micro-particles, PLGA, HPLC, Pharmacokinetics, Vitamin B2, Riboflavin, Drug Delivery System, In vivo Release.

الملخص

هدفت الدراسة الحالية الى تحسين تقنية سريعة وقابلة للتكرار وموثوقة وفعالة لتقدير النشاط البيولوجي لفيتامين بي 2 في حقن جرعة باستخدام تقنية كروموتوكرافيا سائلة عكسية عالية الاداء , تمت الموافقة على بوليمر كمكون نشط و قابلة داخلية, حيث تم تحميل الفيتامين على نوع بوليمر حامض اللاكتيك مطعم في بوليمر حامض الكلايكولك بنسبة 50:50 , وتم حقن حجم 1ملغم من البوليمر المحضر. في الحيوانات التي هيئت للحقن وهي الجرذان بكلا الجنسين المؤنث والمذكر. بشكل فردي ، وصلت المدة الزمنية للحيوان المستضيف إلى 40 يومًا, وسُجل نشاط فيتامين بي 2 في ساعات سريعة خلال ستة اسابيع بواسطة جهاز كروموتوغرافيا سائلة عكسية عالية الاداء لعينة البلازما. تشير النتائج إلى أن جميع التركيبات تستجيب بشكل مستمر خلال أربعين يومًا ، مع اكتشاف أفضلها وفقًا للتوافر الحيوي للدواء داخل النطاق المسموح به, بلغ افضل اداء مسجل في فابس الى نسبة 108.

الكلمات المفتاحية: الصيدلة الحركية, فيتامين بي2, الرايبوفلافين, نظام توصيل الدواء, اطلاق سراح داخلي و بي ال حي اي.

Biological Activity of Rats Treated with Riboflavin in Polymeric PLGA as Injectable Form

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النشاط البيولوجي في الجرذان المعاملة بالريبوفلافين المحقونة بالبوليمر (بي ال جي اي)

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The brain will not be affected by an electric shock unless the entry point was the head. Otherwise, an electric shock will daze the person or can short-term amnesia, respiratory arrest or seizure, while the heart is sensitive to an electric shock that will disrupted the heart rhythm and burned soft tissues and decreased blood pressure which affected electrolytes balance which lead to the failure of the kidneys.

The kidney is the only organ responsible for the removal of all damaged tissues of the skin and other organs of the body which will put a heavy load on the functions of the kidneys, especially the removal of all fatty deposits

Most studies concerning electric shocks concentrate on liver, while they are very limited studies concerning the effect on heart and kidneys.

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which lead to disorders such as achalasia, Allgrove syndrome, gastroparesis, pyloric stenosis, functional dyspepsia and unexplained nausea, vomiting and diarrhea (Dellon and Ringel, 2006; Abell *et al*., 2009).

Long term effects

It is very hard to diagnose long-term effects of electric shock on the human body, but in general, the victim will feel eye problems, generalized pain and joint stiffness with itching. The victim will face psychological effects such as reduced cognitive abilities, post-trauma stress disorder (PTSD) and anxiety

Conclusion

The electrical resistance of the human body depends upon the long duration of electric contact, type of the current (AC or DC), intensity of the current (amperes/voltages), sites of entry and exit points, wet or dry body, individual metabolism of the person, sweat glands activity, human body mass, type of the tissue it travels through and its resistance, the amount of lipids and fats in that tissue and the general health of the person.

Identifying entry and exit sites after electric shock is very difficult and the survival of the person depends solely on the efficiency and rapidity of medical treatment.

In most cases, the liver showed portal vein thrombosis, biliary duct enlargements with beginning of cholangitis (inflammation of a bile duct) and pneumobilia (A presence of air bubbles in the biliary tree). The presence of air bubbles leads to inflammatory and the presence of bacteria inside biliary tree

Respiratory system

If a high electric current hit the lungs directly, severe visceral injuries can occur. The respiratory system can be paralyzed and the heart-beat can either become very fast and irregular or can completely stop beating (Fineschi *et al*, 2006).

Burns may occur in lower lobes. The injuries can be fatal unless life-saving treatment was applied. Due to the few cases, the pathogenesis is not entirely understood (Karamanli and Akgedik, 2017; Nizhu *et al*, 2020; Chen *et al*, 2021)

Kidney injuries

High tension electricity can causes massive necrosis to all deep structures such as muscles, vessels and nerves and these may lead to acute renal failure. The kidney is the only organ responsible for the removal of all damaged tissues of the skin and other organs of the body, and this will put a heavy load on the functions of the kidneys, especially the removal of all fatty deposits (Chauhan *et al*, 2004; Ho *et al*, 2020; Teramoto *et al*, 2020).

Digestive system

The gastrointestinal (GI) system coordinates electrical activity through the tract. Normal mechanical functions depend on the highly coordinated activity of this electrical excitation, whose disruptions can lead to disorders, but not life-threating (Tse *et al* 2016).

The growth of intestinal cells' bacteria is affected by electric currents and electromagnetic fields generated by the smooth muscles of the small intestine (Camilleri *et al*, 2006). A severe electric shock may affect GI motility

balance and this will lead in most cases to the failure of the kidneys (Tse *et al*, 2016).

If a low electr0ic currency passed through the body, only tingling or buzzing sensation can be felt, but no injury.

In general, muscles, ligaments and tendons will be tear and burn as a result of the electric shock. When a current travels through flexor muscles, such as those present in forearms, the fingers will have sustained contraction and closed. The victim will not be able to let go of the source of the current, making the duration of the contact longer and increasing the severity of the shock (Lund *et al*, 2000; Manegold *et al*, 2007).

A violent spasm occurred when an electric current travels through extensor muscles. The victim will be propelled many meters away if an electric current passes through hip extensor muscles and lengthen them (Lund *et al*, 2000; Perret *et al*, 2009).

Microorganisms after burns with electric current

Biofilms are invisible communities of microscopic microorganisms that can be found anywhere and everywhere in moisture, nutrients and surfaces. After an electric shock, microorganisms will be growing rapidly inside the burns of a human's skin. Biofilms should be treated quickly before causing further harm to the body. Antibiotic treatment not only prevent the infection of the skin, but prevent a potential infection of the necrotic areas located in the inner structures (Kennedy *et al*, 2010; Song *et al*, 2016; Guest *et al*, 2020; Comerci, 2022; Hussain *et al*, 2022;).

Pseudomonas aeruginosa was the most bacteria isolated from the wounds caused by electricity (Fineschi *et al*, 2006; Kunwar *et al*, 2021).

medications (antidepressant mostly). It did not harm the brain but can cause a kind of (amnesia, headache or fatigue). It bothersome and irritate the person and do away after few weeks (Papp and Onton, 2018; Papp *et al*, 2022).

Heart injuries

The pulses of the heart are controlled by electrical impulses (cardiac action potentials) generated from (pacemaker cells). These cells are located in the sinoatrial (SA) node situated in the back wall of the right atrium. These cells are the natural pacemaker.

It is impossible for outside electric current to interfere with the pulses of heart unless it was directed to the heart (Priori *et al*, 2005; Farwell and Gollob, 2007).

If a weak electric current was passed through the chest, it can result in ventricular fibrillation. If the treatment was delayed, this will become lethal since the heart muscle cells will be moved independently and a cardiac arrest can occurred.

If electric current was high, it will interfere with the rhythm of electric pulses of the heart causing (arrhythmia) or a (cardiac arrest) leading to the death of the person (Pawlik *et al*, 2015; Chen *et al*, 2016; Waldmann *et al*, 2018).

The heart is sensitive since an electric shock can disrupt the heart rhythm, and for this reason, controlled electric shocks are used medically as a treatment to restore normal sinus rhythm (NSR).

Muscles

High level shocks will burn all soft tissues and induce a muscle contraction which will decrease blood pressure which affects electrolytes

dendrites. This back-propagating electrical pulse helps the synapses know when to strengthen or weaken by helping the synapses figure out when an input signal led to an output spike (called spike-timing-dependent plasticity or STDP) (Smith and Otis, 2003, Naundorf *et al*, 2006; Kole *et al*, 2007).

While the other exception happens experimentally when the end of an axon is stimulated electrically to the spiking level, a full spike will travel backwards towards the cell body, called an "antidromic spike." This doesn't happen normally in the brain and has to be triggered artificially (Scot *et al*, 2007, Shu *et al*, 2007).

The nerves have low electric resistance and when nervous system was affected by external electricity current, a pain, tingling, and numbness and weakens occurred, but it can be recovered quickly. In severe case, the central nervous system can be affected to the extent of causing amnesia, seizure or respiratory arrest (Kole *et al*, 2007; Shu *et al*, 2007).

In general, the brain will not be affected unless high voltage electric current will hit the body, since CNS as a whole consumes the electricity. In most severe cases, the brain may be affected immediately or weeks will be passed before the effectiveness can be shown. Short-term memories region can be affected immediately while long-time memories region remains unattached. The electric current travels among the neurons slowly and in one direction and the information required is carried in the form of alternating current (Kress and Mennerick, 2009).

Sometimes, it is possible to experience an (electric shock) within the nervous system and this known as (brain zap).

The brain zap is an electric shock with dizziness or disoriented and occurs mostly as a side-effect when a person stops taking certain long-time

Fig.3. Penaeus monodon

In humans and other mammals, the nerve signals travel about 120 meters/second, while the fastest nerve signals are found in *Penaeid* shrimp (*Penaeus monodon*) which reach 210m/s. Theses speeds are so low comparing to the speed of an electric wave (few meters to few kilometers per second)(McGraw *et al*, 2001; Emerenciano *et al*, 2022).

Axons and dendrites can, in fact, carry signals in both directions, but they don't due to the asymmetric structure of the synapses and the different signal propagating properties of dendrites vs. axons (Kim *et al*, 2019, Lovaglio *et al*, 2019).

Another factor in the directionality of neurons is that dendrites propagate signals differently from axons. Dendrites are structured to propagate low-voltage analog signals, whereas axons propagate (relatively) high-voltage "binary" pulses. This is due to the slightly different signal amplifying molecules on the dendrites vs. the axons.

There are two exceptions in which signals propagate backwards, one happens naturally. When the neuron fires, not only does a big pulse travel down the axon, but also a small pulse travels in the reverse direction on the

differences, between axon cytosol and the extracellular matrix.

Healthy cells have a membrane potential of ≈≈ 60–70 mV, all using an Na+- K+ pump (Na+/K+-ATPase), driven by ATP energy.

The protein molecules (with the cellular membrane) bind three ions of sodium. During activation, the three ions of sodium were rejected and two ions of potassium will move inside the cell as can be seen in the following figure, and this will produce a wave of successive charge potential changes, moving along the neuron's axon. (Pivovarov *et al*, 2019).

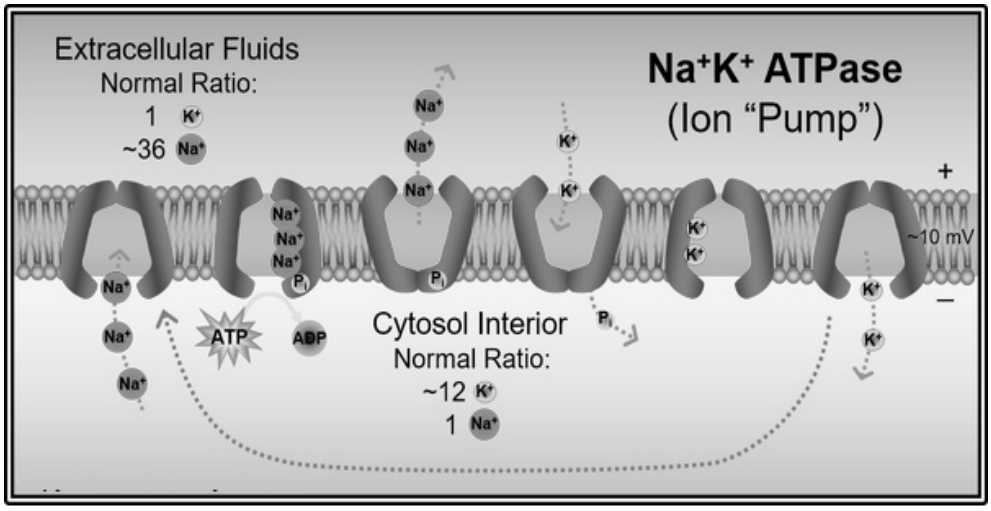

Fig.2. Sodium–Potassium Pump

It flows only forwards and not in both directions due to two reasons: a quick potassium-driven repolarization below threshold levels and due to the refractory period of sodium channels who stay inactivated for long enough to let the action potential pass by.

short-term amnesia, respiratory arrest or seizure.

In rare cases, the damage to the brain or nerves can develop up after several weeks/months of an electric shock and that will depend largely on the extent of the injuries (Cao, 2014; Berg, 2019).

Neurons receive and generate electrical impulses by electrochemical reactions which transmit information that evolved elaborate mechanisms for generating electrical signals based upon the flow of ions across their neuronal plasma membranes, even though they are not intrinsically good conductors of electricity. This is occurred because neurons, like all cells, maintain different concentrations of electrolytes cross their cell membranes (Bean, 2007; Berg, 2019).

At resting phase, neurons initially are permeable to potassium ions (K+), while impermeable to sodium ions (Na+), so due to this and other few reasons, a net negative charge develops on inner axoplasm and a net positive charge develops in the fluid outside the axon. This develops a potential difference called resting potential.

When a stimulus is applied, (whether is mechanical, thermal or chemical), the permeability of the axon membrane increases for Na+ leading to rapid influx of Na+ ions followed by reversal of polarity at that site and hence it is depolarized (Ladurner *et al*, 2005).

This depolarization works as a stimulus for the adjacent region of the axon which continues leading to flow of impulse in the form of "Electric current", so, neurons work like little chemical batteries that produce ions which set up an electrical potential.

There is a slight difference between neurons and a battery, since scientifically neurons do not conduct electricity, since what is traveling along axons are not electrons, but "waves" of rapidly changing ionic charge

hard to heal since all the internal organs of the body lack nerves connected to the pain center of the brain, so the electrified person feel nothing. The burns of the interior organs can cause the production of a high amount of wastes that can cause serious kidney problems (Alivandi and Ehadi, 2007; Cao, 2014)

Liver

The liver is the first organ suffers from an electric shock, it should be evaluated first. The hepatocytes, in case of high voltage electricity that creates heat, can be easily damaged which (may) lead to necrosis.

In most cases, the liver showed portal vein thrombosis with thick walls, biliary duct enlargements which show the beginning of cholangitis (inflammation of a bile duct) and pneumobilia (A presence of air bubbles in the biliary tree). The presence of air bubbles leads to inflammatory and the presence of bacteria inside biliary tree (Sherman and Tran, 2006, Yildiz *et al*, 2011).

A polymorphism of hepatic lesions (such as biliary tree lesions, portal thrombosis, necrotic lesions and abscesses) was, sometimes, affected the person. Thrombosis can be either occurred by excessive activation of the coagulation cascade on the external pathway or due to the damage of vascular branches with extensive endothelial lesions caused by an electric current. If the treatment was slow, necrotic lesions of the liver will be replaced by fibrosis scars or cysts resulting in (multiple hepatic abscesses) which inhibit (to several extents) the defense mechanism of the liver (Ladurner *et al*, 2005; Ponziani *et al*, 2010).

Nervous system shock

The brain will not be affected by an electric shock unless the entry point was the head. Otherwise, an electric shock will daze the person or can

The survive of the person depends solely on the efficiency and rapidity of medical treatment since the heat produces by electricity current can cause necrosis and destructions of cell membranes (Fish *et al*, 2009).

The heat produces during electric current passage depends greatly on the amount of the resistance. With high resistance, a rapid increase of heat occurs with a great damage to the tissues (formation of lesions) located along the path of the electric current.

The less resistance organ may escape injuries or has a minimum amount of them, but the electric current (when pass through it) may cause greater damage to other internal organs (Fish et al, 2009; Alnuaimi *et al*, 2011).

In general, and according to Joule's Law, the amount of the damage of the tissues is proportional with the square of the intensity of the electric current (I) as in the following equation:

$$Q=I2\cdot R\cdot t \quad \text{.....................................}(1)$$

Where generated heat (Q) is equal to the square of the intensity (I) multiplied by resistance (R) and time (t).

This equation explains the importance of an increase in the amperes determines multiple extensive lesions than an increase in the voltages (Guler and Seyhan, 2001; Kulkarmi and Gandhare, 2015).

Burns to tissues and organs; cardiac arrest, muscle spasms, damage to nervous system, and other unexpected consequences can be caused by an electric shock.

External burns can be treated entirely, but internal burns of organs are

but embedded inside the body. In electric injury, the point of entry is situated far away from the point of exit (Bailey *et al*, 2019).

The wounds of both entry and exit could be severe, so it's essential for the physician to try hard to identified enter and exit wounds which is not an easy task at all especially with the internal damage inside the body, so it is recommended that the patients suffer from electric injuries must be put under observation for a week to understand the prognosis fully (Fish and Geddes, 2008; Daskal *et al*, 2019).

It is important to emphasis that the damage of the tissues increased with the increase of amperes especially at the entry and the exit points of the current. It was noticed the presence of edema, coagulations and swelling of muscles at these points (Sherman and Trans, 2006; Kim *et al*, 2019; Lovaglio *et al*, 2019).

Burns of the tissues

Several factors affect the resistance of the body such as the type of the organ's tissues, so blood vessels and nerves have low resistance, while bone and skin have high resistance.

The dry skin has a high resistance which results in extensive superficial burns but limiting deeper conduction of harmful current comparing with wet moisture skin.

Superficial burns can occur (even with a lower voltage) on the surface of the skin, but high voltages may cause internal burns (which are difficult to heal) leading to the failure of an organ in the body. This may lead to death (Markiewicz-Gospodarek *et al*, 2022).

An electricity current of 0.25 milli-amperes (mA) will not affect the body, while electricity current above 10mA travels (through the muscles of the hand) will causes fingers to contract and hold the source of the current firmly and this will increase the time of contact between electricity current and the muscles which will increase the severity of electrocution.

If the electricity current travels (through the muscles of the legs), it will causes the extended of the limbs due to the burning and ruptured of tendons and ligaments which explained why the victim will be propelled many meters away. In many experiments, it was shown that skeletal muscles sustained the largest temperature rise and then heated adjacent tissues. (Khelif *et al*, 2003; Cheung *et al*, 2013; Cheng, 2015(.

Entry and exit sites

There are always two burns' sites in the body referred to them as (Entry and exit sites). It indicates that the electric current will enter the body from one point and exit it from another point, for example, current will enter through the finger of one hand and exit from the finger of the other hand.

Actually, the flow of an electric current through the body follows two paths: the surface of the skin and along the blood circulatory system.

These two terms are confusing since the electric current will change direction many times during a second or two seconds as soon as it enters the body depending on the resistances of tissues (Bailey *et al*, 2019; Deng *et al*, 2021).

These two terms are confusing too since they can be compared with entry and exit points of a bullet. The entry and exit points of a bullet are opposite each other in the body and in many times, the bullet will not exit

The electric resistance of a human body depends upon several factors such as the long duration of electric contact, type of the current (AC or DC), intensity of the current (amperes than voltages), sites of entry and exit points, wet or dry body, individual metabolism of the person, duration of time, sweat glands activity, human body mass, the type of the tissue it travels through and its resistance, the amount of lipids and fats in that tissue and the health of the person (Miller and Zachary, 2017).

This create a lot of problems during the investigation of electric current related accidents, since the electrical engineer thinks only in term of the applied-amperes and voltages applied, while but the physician thinks of paths in which current flowed inside the body (Mondal and Keisling, 2013; Meng *et al*, 2016).

Any body organ which is found close to the direct path of electricity will be likely to be affected and death can occurs easily if an electric current passed from the right arm and move towards the end of the leg. In other words, the electricity will pass directly through the chest cavity.

The brain does not be affected unless the electric current (in rare occasions) enters from the skull (Cao, 2014; Meng *et al*, 2016).

So most of the time, the organs within chest cavity are mainly affected as a result of an electric shock. These include heart, lungs, kidneys, intestines, lever etc. An electric shock may directly cause death in three ways: paralysis of the breathing center in the brain, paralysis of the heart, or ventricular fibrillation (uncontrolled, extremely rapid twitching of the heart muscle). It is generally believed that ventricular fibrillation is the most common cause of death in electric shock (Mondal and Keisling, 2013; Meng *et al*, 2016).

AC and DC

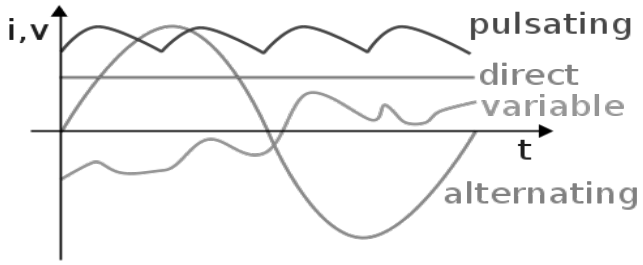

Fig.1. Types of electric waves

Two types of electrical currents are used: An alternating current (AC) and direct current (DC).

AC is an electrical current that reverses the route of electron flow numerous times every second. It main use is to feed houses and most commercial centers.

DC is an electrical current that flows in one direction-route. Its main use is in car batteries, medical appliances like defibrillators and other low voltage applications.

Both types can cause tetany (spasms or seizing), cardiac fibrillation, respiratory muscle paralysis and cardiac dysrhythmia upon electrical shock, but AC is considered the more dangerous, since the body can tolerate DC more than AC (Song and Wang, 2014; Xiu and Loul, 2016).

Severity of electric injuries

The severity of electric injury depends on the electrical resistance of the human body which can alter considerably during the passage of an electric current.

people (suffered from electrical injuries) to emergency wards or burn units. It was emphasized that the extent of electric-burns is more severe compared with non-electrical burns. For this reason, all experiments (past and present) used different kinds of animals as well as postmortem studies for the bodies who died by electrocution (Torres-Duran, 2006; Agbenorku *et al*, 2014; Abbate *et al*, 2022).

The objective of this review is to show different paths that an electric current can take to pass through the body, and how this current can be conducted and how can influences the nature of injuries and their types.

Electrical injury

It is defined as any physical harm to the body caused by electric current. This harm can be light tingling sensation or severe destruction of skin and organs, pain and may be death.

Dry human body has high resistance and will allow less current to flow, while wet body has low resistance to electricity.

Tissues (skin, bone, muscles, tendons, corneas, etc.) must be recovered quickly after electrical injury, usually between 12–24 hours after the electric shock (Agaa *et al*, 2016).

Accidental electric shocks can occur without any intention. Most children will have an electric shock by touching bare live wires or tried to put metal needles through the openings of electric sockets for fun, while adults can hit by electricity during cleaning electric instruments or trying to replace faulty sockets. Sometimes, a person can get lucky when the electricity throws him/her away or that person could pull away from the live current and survive (Arnoldo and Purdue, 2009; Soar *et al*, 2010).

Introduction

When the first commercial electric lines were established, people were killed due to accidently misuse of electricity. The first accident with electricity leads to death happened when a stage-carpenter in Lyon, France touched 250-volts AC generator in 1879. Since then, universities and medical establishments began to conduct studies to understand the effects of electricity on human beings (Liu, 2018; Kunwar *et al*, 2021).

Different effects of electric shock were tried to evaluated which were defined in a simplest way as (a sudden violent response to electric current flow through any part of a person's body) and various theories concerning suspended animation and action of electricity on the central nervous system were proposed (Cerri *et al*, 2013).

When the electric current passes through the body, whether direct (AC) or alternating (DC) electric current, it causes tissue damage which are known as (Primary electrical injuries), while (second electric injuries) are the injuries caused by the falling of the person and hitting the floor forcibly.

In contemporary time, there is a wide dependence on electricity which can lead, if the necessary precautions are not met, to different types of accidents (some of them are deadly). For this reasons, an understanding about the work of electric current paths through the body can be of great help to any clinic which can minimize any medical and surgical problems (Fineschi *et al*, 2006; Agaa *et al*, 2016).

According to World Health Organization (WHO), four people are killed every week by electrocution in the last decade with the admission of 3% of

يعتمد بقاء الفرد على قيد الحياة على كفاءة العلاج الطبي وسرعته، ويعد الكبد أول عضو يتأثر بالصدمة الكهربائية، مما يؤدي الى عدة اعراض منها تخثر داخل الوريد البابي-الكبدي، وتضخم قناة الصفراء، وتكون فقاعات هوائية داخل الأوعية الدموية للصفراء.

بصورة عامة، لا يتأثر المخ بالصدمة الكهربائية الا اذا كانت نقطة الدول هي الرأس، ولكن ستؤدي الصدمة الكهربائية الى حالة من الذهول أو فقدان الذاكرة على المدى القصير، او توقف التنفس، بينما يتأثر القلب بالصدمة الكهربائية التي يمكن ان تعطل نظام القلب، وتحرق الأنسجة الرخوة، وينخفض ضغط الدم، كما تتأثر الكلية بشكل كبير لكونها المسؤولة عن ازالة جميع انسجة الجسم التالفة بالصدمة الكهربائية، وازالة الرواسب الدهنية.

من الصعب تشخيص الآثار بعيدة المدى للصدمة الكهربائية، ولكن بشكل عام، سيشعر الفرد المصاب بمشاكل في العين، والم عام، وتيبس في المفاصل مع حكة شديدة، وتتضمن الآثار النفسية ضعف القدرات المعرفية، واضطراب ما بعد الصدمة والقلق المبالغ به.

الكلمات المفتاحية: Lesions, Synapses, Cirrhosis ,Electric necrosis, Entry and Exit Points

tissues and decreased blood pressure which affected electrolytes balance which lead to the failure of the kidneys.

The kidney is the only organ responsible for the removal of all damaged tissues of the skin and other organs of the body which will put a heavy load on the functions of the kidneys, especially the removal of all fatty deposits

It is very hard to diagnose long-term effects of electric shock on the human body, but in general, the victim will feel eye problems, generalized pain and joint stiffness with itching. The victim will face psychological effects such as reduced cognitive abilities, post-trauma stress disorder (PTSD) and anxiety

Keywords: Lesions, synapses, cirrhosis, electric necrosis, entry and exit points.

المستخلص

يتم قتل اربعة اشخاص كل اسبوع صعقاً بالكهرباء خلال العشر سنوات الماضية حسب منظمة الصحة العالمية، ويتم علاج 3% من الأفراد (الذين يعانون من اصابات كهربائية) سنوياً في اجنحة الطواريء في المستشفيات.

تعتمد شدة الأصابة الكهربائية على مقاومة جسم الأنسان للكهرباء على عدة عوامل أهمها مدة التلامس الكهربائي الزمنية، ونوع التيار (مستمر او متردد)، وشدة التيار (أمبير/فولت)، ونقطتي دخول التيار الكهربائي وخروجه، ومدى جفاف الجسم او رطوبته، والتمثيل الغذائي للفرد، ونشاط الغدد العرقية، وكتلة الجسم، ونوع الأنسجة التي ينتقل عبرها التيار الكهربائي ومقاومتها، وكمية دهون الجسم، والصحة العام للفرد.

مصطلح نقطتي دخول التيار الكهربائي وخروجه محير، لعدم تقابل النقطتين داخل الجسم، نظراً لقيام التيار الكهربائي بتغيير اتجاهه عدة مرات داخل الجسم، واعتماداً على مقاومة الأنسجة والأعضاء للتيار الكهربائي.

Abstract

According to World Health Organization (WHO), four people are killed every week by electrocution in the last decade while 3% of people (suffered from electrical injuries) were admitted to emergency wards.

The severity of electric injury depends on the electrical resistance of the human body which depends upon several factors such as the long duration of electric contact, type of the current (AC or DC), intensity of the current (amperes/voltages), sites of entry and exit points, wet or dry body, individual metabolism of the person, sweat glands activity, human body mass, type of the tissue it travels through and its resistance, the amount of lipids and fats in that tissue and the general health of the person.

Entry and exit sites of an electric current are confusing since the electric current changes direction many times during entering the body depending on the resistances of tissues and organs.

The survival of the person depends solely on the efficiency and rapidity of medical treatment especially as the liver as the first organ suffered from an electric shock and should be evaluated first. In most cases, the liver showed portal vein thrombosis, biliary duct enlargements with beginning of cholangitis (inflammation of a bile duct) and pneumobilia (A presence of air bubbles in the biliary tree). The presence of air bubbles leads to inflammatory and the presence of bacteria inside biliary tree

The brain will not be affected by an electric shock unless the entry point was the head. Otherwise, an electric shock will daze the person or can short-term amnesia, respiratory arrest or seizure, while the heart is sensitive to an electric shock that will disrupted the heart rhythm and burned soft

The Effect of An Electric Current on Human Body (A Review)

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(مقالة مرجعية)

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م. م. مها رعد هاشم السامرائي،
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