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Effect of drugs, medicinal herbal substances, fruits, coffee and tea on renal vessels in patients with and without renal failure[1]

تأثير الأدوية، الأعشاب الطبية، الفواكه، البن والشاي على الأوعية الدموية الكلوية في مرضى بالفشل الكلوي وبدونه [2]

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ABSTRACT:

Objective and Methodology: This study conducted in Al-Dhalea, Yemen, aimed to identify narrowed blood vessels, assess collateral circulation, and treat vascular stenosis and kidney failure. A randomized observational study was used to evaluate intrarenal vascular stenosis and signs of kidney failure. The sample included 476 patients (153 males, 323 females) aged 31–76 years, with data entered into a computerized system.

Results: Feedback and laboratory tests for creatinine levels showed rapid patient improvement. Renal arteries widened, arcuate arteries appeared, and lobar arteries elongated to near-normal levels within 30 minutes of medication. Creatinine levels normalized within two weeks, and fibrosis-like whitening disappeared by the third week of treatment.

Conclusion:

1-Treating intrarenal vascular stenosis and kidney failure is now possible. 2-Medications, herbal remedies, fruits, vegetables, and drinks significantly influence cytokine and chemokine levels within 5–10 minutes. 3-Clopidogrel 150 mg and low-dose statin 10 mg outperform aspirin 75 mg, clopidogrel 75 mg, and statin 10 mg during periods of aspirin's adverse effects. 4-Clopidogrel (two tablets) and low-dose statin can open narrowed renal arteries and normalize kidney function. 5-Clopidogrel (two tablets) is safe if patients avoid raw ginger and garlic and discontinue use 5–7 days before menstruation.

Keywords: Clopidogrel 150 mg, Statin 10 mg, treatment, kidney failure, narrowed arteries

المستخلص:

الهدف والمنهجية: استهدف البحث-الذي أجري في محافظة الضالع بالجمهورية اليمنية- تحديد الأوعية الدموية المتضيقة ووجود الأوعية الاحتياطية، بالإضافة إلى معالجة التضيقات الوعائية والفشل الكلوي. اعتمد البحث على دراسة ذات ملاحظة عشوائية لرؤية التضيقات الوعائية داخل الكلوية وعلامات الفشل الكلوي ومعالجتها، وشملت العينة 476 مريضًا (153 ذكورًا، 323 إناثًا) بأعمار بين 31-76 عامًا، وتم إدخال البيانات إلى برنامج حاسوبي.

النتائج: أظهرت التغذية الراجعة والفحوصات المخبرية للكرياتينين أن المرضى شهدوا تحسنًا سريعًا في حالة الشرايين الكلوية مع اتساعها وظهور الشرايين القوسية واستطالة الفصية للمستوى الطبيعي خلال 30 دقيقة من تناول الأدوية. عاد مستوى الكرياتينين إلى الطبيعي خلال أسبوعين، واختفى الإبيضاض الشبيه بالتليف في الأسبوع الثالث.

الاستنتاجات:

1. أصبح علاج التضيقات الوعائية الكلوية والفشل الكلوي ممكنًا.
2. الأدوية والأعشاب والأطعمة تؤثر بسرعة على السيتوكينات والكيموكينات.
3. كلوبيدوجريل بجرعة 150 ملجم وستاتين 10 ملجم يتفوقان على الأسبرين 75 ملجم في فترات تأثيره السلبي.
4. كلوبيدوجريل بجرعة حبتين وستاتين بجرعة منخفضة يساعدان في فتح الشرايين الكلوية المتضيقة واستعادة وظائف الكلى الطبيعية.
5. استخدام كلوبيدوجريل بجرعة حبتين آمن إذا تجنب المرضى تناول الزنجبيل والثوم الني وتم إيقافه قبل الدورة الشهرية بـ5-7 أيام.

الكلمات المفتاحية: كلوبيدوجريل 150 ملجم، ستاتين 10 ملجم، معالجة، الفشل الكلوي، الشرايين المتضيقة.

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2-توثيق الاقتباس (APA): الأشول، نشوان صالح محمد، (2024). تأثير الأدوية، الأعشاب الطبية، الفواكه، البن والشاي على الأوعية الدموية الكلوية في مرضى بالفشل الكلوي وبدونه، *مجلة مركز جزيرة العرب للبحوث الطبية والتطبيقية*، 1 (2)، 100- 125. https://doi.org/10.56793/pcra23126

1-Introduction.

Renal failure cases are rising globally each year due to infection, ischemic, and inflammatory processes, with current treatments limited to dialysis or transplantation. This underscores the urgent need for medical therapies that improve renal function and vessels, easily monitored for effectiveness.

Renal vessels, like any in the body, are prone to stenosis caused by conditions such as atherosclerosis, fibro muscular dysplasia, or autoimmune inflammation, leading to temporary flank pain and eventual renal atrophy. In previous research, doppler ultrasound revealed common intracranial vascular issues in both healthy individuals and renal failure patients, including stenosis, obstruction, and vessel disappearance, often starting at the renal poles. These findings emphasize the vascular origins of renal failure and guide therapeutic monitoring.

This study focuses on treating intrarenal vascular stenosis and monitoring changes using doppler color flow ultrasonography. Renal function was assessed through creatinine levels in patients, all of whom likely had SARS-CoV-2 sequelae from 2019 to 2023. The therapeutic regimen combined drugs, medicinal herbs, home herbal substances, and specific fruits and vegetables to evaluate positive effects (symptom relief) or negative effects (symptom worsening). Additional monitoring included SpO2% and PI%, doppler visualization of vascular improvements, and pre- and post-therapy creatinine measurements.

2- Research Methodology and Materials:

This study involved an observational, random sample of 476 patients (153 males, 323 females, aged 31—76 years). Sonography and color flow doppler imaging were used to detect intrarenal vascular stenosis and monitor renal function improvements. SpO2% and PI% were measured using a fingertip oximeter for early therapeutic effects, and creatinine levels were analyzed for renal function changes.

The treatment included clopidogrel 150 mg, statin 10 mg, and various drugs, herbs, and natural substances like fruits and beverages. Data was recorded and analyzed to assess renal vascular and functional improvements, including fibrosis reversal, over three weeks. The study was conducted at Dr. Nashwan Al-Ashwal Clinic for Medical and Cardiac Diseases in Adhale, Yemen, from June 12, 2022, to June 30, 2023.

Patients were divided into two equal groups (A: 238, B: 238) and monitored at intervals (5—10, 15, 30, 60 minutes, and two hours) to evaluate which regimen produced the best results in improving renal blood flow.

Monitoring of improvements; positive effects if patients improved, and negative effects if patients suffering of worsening of manifestations, or worsening of renal blood vessels state using the following parameters:-

1- Improvement or worsening in clinical manifestations
2- Improvement or deterioration in SpO2% and PI% that measured by fingertip pulse Oximeter
3- Color flow Doppler imaging of renal blood vessels

The following steps were used in pre and post therapeutic periods:

1- B-mode, Color flow and spectral doppler ultrasonography at zero time (in pre therapeutic), then at 30 and 60 minutes, then at end of two hours, and at 7th day, and day 21 in post-therapeutic period; to see intrarenal blood vessels, collateral vessels, and measure velocity and systolic/diastolic ratio of blood flow in intrarenal arteries from hilum to cortex, and diastolic slope at cortical level.
2- Fingertip pulse Oximeter for measuring of SpO2%, PI% in all ten fingers at zero time, 5 to 10 minutes and 15, 30, & 60 minutes then at end of two hours after the first dose of drugs, herbs and home herbal substances.
3- Complete blood count at zero time
4- Renal function test; plasma creatinine level at zero time and 3rd to 7th day post therapy

5- Blood sugar, HbA1c at zero time and on day 21 of therapy.
6- Blood pressure level measurements at zero time, 30 minutes after first dose, and day 7 of therapy.
7- Asking patients to record any changes in their manifestations or any new symptoms during first 30 to 60 minutes after first dose.
8- Update in therapeutic regimes was achieved according to change in SpO2% & PI% by fingertip pulse Oximeter of all fingers of both hands, after 5 to 10 minutes, and 15, 30, 60 minutes and two hours of last drug or medicinal herbal substance used, and by its results the appropriate therapy and routes of administration were chosen.
9- Update of regime is depend on the new regime for patients with SARS-CoV-2 variants sequel used in a parallel study that take care and follow up of this subject since its emergence.

Therapeutic regimes: there are two regimes: Firstly: For groups A & B; (drugs tablets only):group A (Tablets of Aspirin 75 mg, Clopidogrel 75 mg & Atorvastatin 10 mg); given Aspirin at first, then clopidogrel after 30 minutes with atorvastatin. group B (Tablets of Clopidogrel 75 mg; two tablets = 150 mg & Atorvastatin 10 mg), clopidogrel and atorvastatin were giving at the same time.

According to the results the best regime was giving to all patients, and added the other drugs, herbs, home herbal substances to the therapeutic regime according to response and change in SpO2percentage and PI%, and to change in manifestations by decreasing or increasing in intensity, and to re-opening of intra-renal vessels.

Table (1) Manifestations of patients and their percentage% from 476 patients

1)breathing difficulty	15%	10)abdominal distension	75%
2) headache	32%	11) Constipation	33%
3) tinnitus	27%	12)Dysuria	6%
4) dizziness	21%	13)Arthritis	19%
5) Eyes puffiness	7%	14)Popliteal fossa bulging	2%
6) renal pain	38%	15)Testis enlargement	1%
7) chest pain	64%	16)Lower abdominal pain	5%
8) lower limbs pain	3%	17) hypertension	35%
9) Epigastric pain	30%	18) hypotension	49%

Laboratory investigation: Complete blood counts, Sugar, HbA1c, and serum Creatinine

Table (2) Drugs and Herbal Pharmaceutical Drugs used in treatment of patients during June, July & August 2022

Drugs & pharmaceutical medicinal herbs	Date of positive, negative and no effects: 2022														
	June				July		August								
	12	13	16	19	17	19	03	04	06	11	14	17	18	19	21
Clarithromycin 250 mg tab															
Amoxicillin 500 mg cap															
Azathioprine 50 mg tab	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Ginkgo biloba 200mg tab chewing	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Echinacea Purpurea cap SL	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Rumalaya forte tab SL	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Vit.D3 with calcium tab SL															
Vitamins A + E Gelatin capsule SL	N	N	N	N	N	N	N								
Septilin Syrup Or Sublingual Tablets	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Clopidogrel 75 mg x2															
Atorvastatin 10 mg tab															
Aspirin 75mg tab swallowing	N	N	N	N	N	N	N	N	N	N	N				

Table (3) Drugs and Herbal Pharmaceutical Drugs used in treatment of patients during August & September 2022

Drugs & pharmaceutical medicinal herbs	Date Of Positive, Negative and No effects: 2022

	August						September									
	22	23	24	25	26	30	01	03	04	07	11	12	13	18	20	26
Clarithromycin 250 mg tab	N	N	N	N	N											
Amoxicillin 500mg cap	N	N	N	N	N											
Azathioprine 50 mg tab SL	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Ginkgo biloba 200 mg SL	N															
Echinacea Purpurea cap SL	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Rumalaya forte SL																
Vit.D3 with calcium tab SL																
Vit. A + E SGC SL																
Septilin tab/syrup SL	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Clopidogrel 150 mg tab																
Atorvastatin 10 mg tab																
Aspirin 75 mg tab							N	N	N	N	N	N	N	N	N	N

Table (4) Drugs and Herbal Pharmaceutical Drugs used in treatment of patients during October & November 2022

Drugs & pharmaceutical medicinal herbs	Date of Positive, Negative and No effects														
	October/2022											November/2022			
	03	06	08	09	14	17	22	24	25	27	29	03	05	06	15
Clarithromycin 250 mg tab															
Amoxicillin 500 mg cap															
Azathioprine 50 mg tab SL															
Ginkgo biloba 200 mg tab SL															
Echinacea Purpurea cap SL	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Rumalaya forte SL															
Vit.D3 with calcium tab SL									N	N	N	N	N	N	N
Vit. A + E SGC SL															
Septilin Syrup/tablets SL	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Clopidogrel 75 mg															
Atorvastatin 20 mg											N	N	N		
Aspirin 75 mg	N	N	N	N	N						N	N	N	N	N
Simvastatin 10 mg plus Ezetimibe 10 mg	N	N	N	N	N	N	N	N	N	N				N	N

Table (5) Drugs and Herbal Pharmaceutical Drugs used in treatment of patients during June, November & December 2022

Drugs & pharmaceutical medicinal herbs	Date Of Positive, Negative and No effects														
	November/2022					December/2022									
	16	22	24	26	29	01	02	05	08	10	14	15	18	25	29
Clarithromycin 250 mg tab															
Amoxicillin 500 mg cap															
Roxithromycin 150 mg tab	N					N	N	N	N	N	N	N	N	N	N
Azathioprine 50 mg tab SL															
Ginkgo biloba 200 MG SL															
Echinacea Purpurea cap SL	N	N	N												
Rumalaya forte SL								N	N	N	N	N			
Vit.D3 with calcium tab SL	N	N	N	N	N	N	N	N	N	N	N	N			
Vit. A + E SGC SL								N	N	N	N	N	N	N	N

Septilin Syrup/tablets SL	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Clopidogrel 75 mg tab+ two tablets															
Atorvastatin 20 mg tab															
Aspirin 75 mg tab	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N

Table (6) Drugs and Herbal Pharmaceutical Drugs used in treatment of patients during Jan, February, April, May & June 2023

Drugs & pharmaceutical medicinal herbs	Date of positive, negative and No effects year: 2023										
	January		February	April	May			June			
	01	17	02	14	04	08	26	01 - 16	17- 20	21 – 24	25 /6 – 15/7
Clarithromycin											
Amoxicillin											
Azathioprine		N	N	N	N	N	N	N	N	N	N
Ginkgo biloba 200MG SL			N	N	N	N	N	N	N	N	N
Echinacea Purpurea cap SL				N	N			N	N	N	N
Rumalaya forte SL				N				N	N	N	N
Vit.D3 with calcium tab SL							N	N	N	N	N
Vitamins A + E Gelatin capsule SL	N				N		N	N	N	N	N
Septilin Syrup /Sublingual Tablets	N	N	N					N	N	N	N
Clopidogrel 2 tablets of 75 mg											
Atorvastatin 1 tablet 20 mg									N		N
Aspirin 75 mg tab	N	N	N	N	N	N	N	N	N	N	N
Rosuvastatin 10 mg tab	N	N	N	N	N	N	N	N		N	N
Simvastatin 10 mg & Ezetimibe 10 mg tab	N	N	N	N	N	N	N	N	N	N	

Table (7) Therapeutic Fluid of marinated home herbal substances in tap water during June, July, August & September 2022

Fluid of marinated home medicinal particles	Route of administration	Date of positive and negative effects; Year 2022														
		June			July		August				September					
		12	16	19	17	19	03	11	14	17	11	13	18	20	26	30
Clove	Eye drops & SL*	+														-
	Eye drops						+		+							-
Clove, Tea & Coffee	Eye drops & SL		+													
	Nasal Moisturizing			+	+											
	Sublingual					+										
Coffee	Eye drops							+	+							
Tea	Eye drops								+							
Cinnamon	Eye drops								+		-					
	Nasal moisturizing & smell										+!!			+*	+	
	Sublingual														+	
	Mix with hot Tea drinks										+	+!	+	+*		
	Mix with hot drinks of Tea & Coffee													+**	+	D
Cinnamon & Coffee	Eye drops									+						
Clove & Cardamom	Nasal Moisturizing												+	+		
	Sublingual													+**		
	Mix with hot drinks of Tea & Coffee													+**		
Tea & Coffee	Sublingual												+			

+! While drinking of hot red tea putting into it small piece of cinnamon causes negative effect, the putting of few drops of marinated cinnamon in tap water into hot red tea drinks resulted in positive effect. +!! Cinnamon marinated in tap water and its container left with no cover in room will give a positive effect by inhalation of room air that saturated with volatile vapor of cinnamon.+* one substance; cinnamon for nose and hot red tea. +** one substance; cinnamon for nose and mixed with hot drinks of two things; tea & coffee. +*** two substances for two different routes in different patients; clove & cardamom via mouth of some patients in addition to cinnamon via nose and mixed with hot drinks that consisted of tea & coffee for others. D; weak positive effect need another things for strength; that are clarithromycin tab and amoxicillin cap drugs.

Table (8) Therapeutic Fluid of marinated home herbal substances in tap water during October & November 2022

Fluid of marinated home medicinal particles in tap water	Routes of administration	Date of positive, negative and no effects/ Year 2022														
		October									November					
		03	06	07	08	09	14	17	22 - 25	27 - 31*#	03	13	18	20	26	30
Clove	Eye drops & SL*															
	Eye drops															
	Nasal moisturizing								+#							
									+##							
	Mix with Hot drink of Tea & Coffee		+													
Tea	Eye drops															
	Drink								+$							
									+**							
	Sublingual								+#					X6		
Cinnamon	Eye drops									+						
										+^						
	Nasal moisturizing & smell		N*	+*		+*	+		-	+	+					
									+**							
	Sublingual		N*				-									
	Mix with hot Tea drinks															
	Mix with hot drinks of Tea & Coffee	D*		+*		+*										
Cinnamon & Coffee	Eye drops															
Clove & Cardamom	Nasal moisturizing							+	+$	+^						
									+$$							
									N							
									-							
	Sublingual															
	Mix with hot drinks of Tea & Coffee						+		-							
	Eye drops										+					
Tea &Coffee	Sublingual								+							
Cardamom	Eye drops															
	Nasal moisturizing															
	Sublingual															
Clove, Cinnamon &Cardamom	Nasal moisturizing				+					+^^						
	Mix with hot drink of Tea & Coffee				+											
Coffee	Drink															

D*means its effect is decreased and strengthen only by addition of drugs; ginkgo biloba and azathioprine.. +* means the effect of the previous home medicinal herbs prescription returns again after faster eradication of the new viral inflammatory effect. (white color/-); means negative effects (deterioration in the manifestation). + means positive effects (improvement of patient condition with decrease to subside of its manifestation. +## patients benefited from nasal moisturizing by clove marinated fluid and by red tea marinated fluid in tap water as sublingual. +$$ patients benefited from nasal moisturizing by clove & cardamom marinated fluid and by red tea marinated fluid in tap water as sublingual. *# all of them benefited from drinking of hot red tea with sugar only, in addition to different marinated fluids and routes of administration.

Table (9) Hot Drinks that used for treatment of patients during June, July, August & September 2022

Hot drinks	Date of positive, negative and no effects/Year 2022														
	June	July	August/2022									September/2022			
	From 12	1-30	05	06	07-10	11	18	19	21	25	26	30	07	11	20	26/9-2/10
Coffee with: ginger, curcuma, tea & clove			+	-	-	-										
Tea (red) with hot water and sugar only			-	-	+	-							+	+		
Coffee with: ginger, curcuma & tea			-	-	-	+										
Coffee with: ginger, curcuma, cinnamon, tea & clove							+	+								
Tea with clove & cardamom									+							
Coffee with: ginger, cinnamon & curcuma											+					
Coffee with: curcuma. Tea & clove												+				
Tea with; clove, cardamom & coffee																
Tea with: coffee, cinnamon, ginger & curcuma												+	+			
Tea with drops of marinated cinnamon in tap water														+		
Coffee & Tea with marinated fluid of cinnamon in tap ware															+	+

Table (10) Hot Drinks that used for treatment of patients during October, November & December 2022

Hot drinks	Date of positive, negative and no effects/ Year 2022									
	October				November				December	
	06 - 13	14 - 21	22	24 - 2/11	03	5-25	26-28	29-30	01-07	08-30
Coffee & Tea with marinated fluid of cinnamon in tap ware	+									
Coffee & Tea with marinated fluid of Clove in tap water	+									
Coffee & Tea with marinated fluid of Clove, Cardamom, Cinnamon	+									
Tea with; clove, cardamom & coffee		+								
Tea (red) with hot water and sugar only			+!!	+*			+	+	+	
Tea with clove & cardamom						+				
Coffee with Sugar					+3	-				
Tea & Coffee			+!!							
Drinking of marinated tea or coffee in tape water										
Fluid of marinated coffee						+		+		

Fluid of marinated tea					+				
Hot drinks again:									
Sweet Coffee with ginger									+

+!! Drinking of hot red tea with Coffee in patients who respond to nasal moisturizing with fluid of marinated Cinnamon in tap water and the others who responded to nasal moisturizing with fluid of marinated Clove & Cardamom in tap water. +* Hot red tea drinking in all patients with applying of different fluid of marinated medicinal herbal particles; some responded to nasal moisturizing by fluid of clove & cardamom, others to fluid of cinnamon, others to fluid of clove into nasal and tea fluid into sublingual that means the drinking of hot red tea constitute a common therapeutic part in addition to other medicinal herbal particles. +3 started the triple routes of effects; mouth (coffee), nasal (marinated cinnamon fluid) and Eye (marinated clove and cardamom fluid).

Table (11) Hot Drinks that used for treatment of patients during Jan, February, March & April 2023

Hot drinks	Date of positive, negative & no effects/ Year 2023										
	January		February			March			April		
	01-06	07-30	12	16	21-04/3	05	06	29	14	18	27-30
Coffee with ginger											
Tea with clove & cardamom		+**				+$		+$$		+	
Tea (red) with hot water and sugar only			+								
Tea with clove, cardamom, coffee, curcuma, ginger & cinnamon, added into it the fluid of marinated tea, coffee & clove in tap water				+							
Tea with clove, cardamom, coffee, curcuma, ginger & cinnamon, added into it the fluid of marinated tea, coffee, clove & cardamom in tap water					+						
Tea with clove, cardamom added into it 2 ml of fluid of marinated tea, coffee, clove & cardamom in tap water									+$$$		
Tea with; clove, cardamom & coffee											+
Coffee with ginger & curcuma											

+* in spite of it and of clove and cardamom marinated fluid for eye drops, and drugs; clarithromycin, amoxicillin, azathioprine, ginkgo biloba, rumalaya forte and Echinacea the increase of oxygen saturation from 60% after all of these medications to 98% is accomplished by Vit. D3 & Calcium by Sublingual.+$, +$$& +$$$ the same hot drinks of tea with clove and cardamom but the difference in the first is the nasal moisturizing by fluid of marinated tea, coffee, clove & cardamom while in the second is the sublingual putting of curcuma, coffee & ginger powders, & in the third there is nasal moisturizing by this marinated fluid in addition to added of 2 ml from it into the hot drinks of tea with clove and cardamom. *+ the cardamom that added into the hot drinks of tea and clove was as opened and closed, i.e. there is a different medicinal substances were extracted from the cardamom seeds, than what extracted from the encased part.

Table (12) Hot Drinks that used for treatment of patients during May & June 2023

Hot drinks	Date of positive, negative & no effects/ Year 2023										
	May					June					
	05-17	18	25-27	28-29	30-02/6	03	07	11-17	20-24	25-26	27-30
Tea, broken & intact clove& cardamom, with piece of cinnamon	+										
Tea & coffee with broken & intact clove and cardamom		+		+							
Tea, coffee, cinnamon intact & broken clove and cardamom			+		+*						
Tea, coffee with 2 ml of fluid of marinated clove, cardamom, cinnamon & coffee						+					
Coffee without sugar							+#				

Coffee, tea, clove & cardamom without sugar		+			
Tea with cardamom			+		
Tea, clove, cardamom and 2 ml of fluid of marinated clove, cardamom and cinnamon without sugar				+	
Tea, coffee, clove, cardamom, and marinated fluid of clove, cardamom and cinnamon without sugar					+

+* started the administration of Eardrops of fluid of marinated cinnamon and coffee in tap water. +# coffee without sugar if added into it sugar or honey the manifestations were worsen, even if added the sugar to plain hot water All the hot drinks are with sugar except that noted without sugar.

Table (13) Home Herbal Substances used in treatment of patient by Sublingual Route of administration during August, September & October 2022 to January, March & June 2023

Home Herbal medicinal particles	Dates of positive, negative, and no effects													
	Year 2022										Year 2023			
	August				September				October		January		March	June
Sublingual& Mouth	17	18	21	25	01	07	11	26	25	29	04 - 06		20 – 17/4	01 - 30
Tea	-	-	+	+*	-	+	-	-	+	-	-	-	-	-
Coffee	-	-	-	+	-	-	+	+	-	+	-	-	-	-
Curcuma	-	-	-	-	-	-	-	-	-	-	+	-	-	-
Cinnamon	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Clove	-	-	-	+*	-	-	-	-	-	-	-	-	-	-
Cardamom	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Curcuma, coffee & ginger	-	-	-	-	-	-	-	-	-	-	-	-	+	-
Dates	-	-	-	-	+	+	-	-	-	-	-	-	-	-
Plums	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Pomegranate	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Cucumber	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Grapes	-	-	-	-	+	-	+	-	-	-	-	-	-	-
Bitter frankincense	-	-	-	-	-	-	-	-	-	-	-	-	-	+

4-RESULTS:

A- Clinically: 476 cases with 376 cases obeyed all the period of study and 100 cases not obeyed after 7 days of therapy, only still on clopidogrel 2 tablets and atorvastatin 10 mg, therefore success is 100% in relation to clopidogrel two tablet and statin 10 mg (either atorvastatin, rosuvastatin or simvastatin). And for whole therapeutic regime is 100% among the 376 patients, and among the 100 patients in the first 7 days of obey. The clopidogrel two tablets and statin low dose is better than aspirin 75 mg, statin 10 mg, and clopidogrel 75 mg, in the times of negative effect by aspirin.

1- increased of renal pain, chest pain, dizziness, shortness of breathing, headache after 30 minutes of starting therapy with Aspirin 75 mg in group A, then started to decrease after 30 minutes of clopidogrel 75 mg and Atorvastatin 10 mg intake, but new symptoms was appeared after one an hour of drugs intake, as tooth ache, chest pain, or dizziness, that subsided after 15 minutes of adding a second tablet of clopidogrel 75 mg.

2- Decreased in blood pressure level by 20/10 mmg for 35% of patients from both groups. In group B, a decrease started from 15 - 30 minutes. While in group A, no decrease in level of blood pressure after one an hour, but it become after one an hour of second clopidogrel tablet ingestion.

3- Increased in blood pressure by10 - 30/0 mmhg in hypotensive patients from both groups, in first 30 minutes after intake of a second tablet of clopidogrel 75 mg, then 30/20 mmhg after 3 weeks of therapy starting for patients with 80/60 mmhg basal blood pressure (49%).
4- Feeling of comfortable urination after 48 hours in 42% of patients from both groups on third day of therapy.
5- Disappearance of lower limbs edema (3%) and eye puffiness (7%) on third day of therapy
6- Returns of some symptoms after 5 days.

B- SpO2% and PI% measures in patients of both groups: Reveals the following:

1- After 30 minutes of aspirin ingestion there is increasing in PI% from 1.1-8.7, with increased in SpO2% from 90 - 95%.
2- After one an hour PI% are from 1.0 to 4.3, with decrease in SpO2% to 94%

C- Ultrasonography color flow results:

1- There are different effects on renal vessels in group A, by Aspirin 75 mg one tablet as seen in (photo b) of figure 1, the blood vessels of intrarenal widened but the collateral vessels disappeared, while after adding of one tablet clopidogrel 75 mg and atorvastatin 10 mg, the intrarenal blood vessels decreased in numbers as seen in photo c of figure 1, but in group B, by clopidogrel 75 mg two tablets; i.e. 150 mg of clopidogrel, and one tablet of atorvastatin 10 mg as shown in photo d, of figure 1, the intrarenal and collateral vessels increased in numbers and extension.

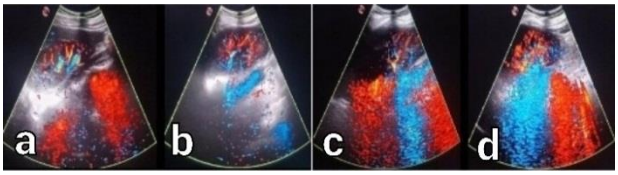

figure 1: a) intrarenal vessels in zero time; presence of interlobar arteries from mid to lower lobe, with no vessels in upper lobe, and few collateral vessels (areas red in color). b) widened interlober renal arteries with increased in smaller and narrower branches but collateral vessels are decreased (areas with blue color and red dors), and disappeared of red color vessels, after 30 minutes post aspirin intake. c)increased in collateral renal vessels (red and blue colored areas), and decreased of intrarenal interlobar vessels from mid level of renal post 30 minutes of one tab of clopidogrel 75 mg and one tab of atorvastatin 10 mg. d) increased in interlobar and interlobular renal vessels from lower to upper poles and in collateral vessels (areas of red and blue colors), post 30 minutes of two tablets of clopidogrel each one 75mg and one tab of atorvastatin 10mg.

2- Reappearance of the not visualized; (post obstructed) intrarenal arterial branches or parts after half an hour of therapy with complete regime till an appearance of whole lengths of intrarenal vessels after 21 days of whole therapy, as shown in figure 2, in opposite to patients that not obliged to whole therapy; only continuing on 150 mg clopidogrel and atorvastatin 10 mg(n=100, 21%) as shown in figure 3.

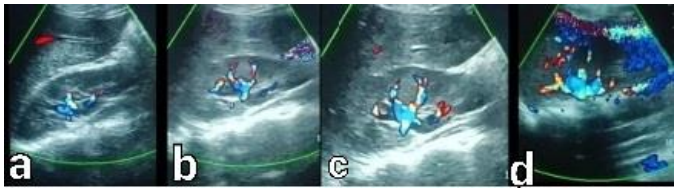

figure 2: a) small parts of interlobar renal vessels in middle renal region only appear at zero time. b) intrarenal arterial flow became visible in interlobar arterial branches all lengths of middle region arteries, and small parts of near to upper pole arteries in addition to small area of collateral vessels near to lower renal pole after 30 minutes. and on day 7 interlobular arteries became more vissible (c), and on day 21 of therapy collateral vessels and intrarenal arteries increased more in length and width (d).

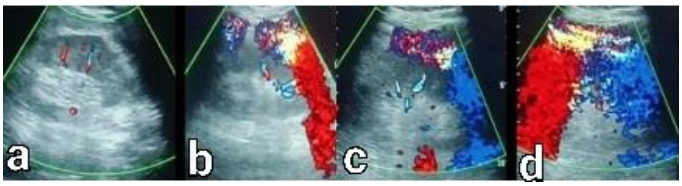

figure 3: patients that not obliged to whole therapeutic regime; interlobar arterial branches and collateral vessels are improved after 30 minutes in (b) with compare to (a). on day 7; there is increasing in color dots which are a transvers areas of interlobar vessels(c). and on day 21, there is increasing of interlobar and collateral renal vessels; but with decrease in width and length of interlobar arterial branches, while the collateral vessels are more visible with large extension in these patients than in those that obliged completely in figure 2.

3- Increased in collateral vascular extension that connected with interlobar vessels in hypertensive patients as shown in figure 3.

4- Both types of collateral vessels the colored (faster) and white vessels (slowest), were disappeared after appearance of large intrarenal vessels as shown in figure 4.

figure 4: in renal failure patients; collateral vessels; (red and green arrows), at base time are visible but no interlobar vessels (a), and from day 7 there is appearance of interlobar vessels and increased in intrarenal collateral vessels while there is decreasing in perirenal collateral vessels (b), continuing improvement in intrarenal interlobar vessels with reappearance of more vessels (c).

5- Improvement in lengths of interlobar vessels and their branches on day 7 of therapy and deterioration on day 21 of therapy but with improvements in collateral vascular extension in patients that re-complain of manifestations return

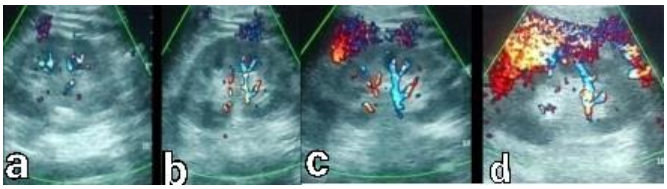

figure 5: interlobar vessels are short and narrowed, and collateral vessels are scant at zero time (a), but started to elongated and wider become after 30 minutes (b), and became more wider and elongated on day 7, with more appearance of collateral vessels (c), while on day 21 the collateral vessels increasing more in extension and the interlobar vessels lost the newly appearing parts and seen as amputated but still connected to collateral vessels (d) a sign that not visible on day 7 (c).

6- Decreased in echogenicity of white blotches in liver, kidneys and perirenal areas on day 21 of therapy.

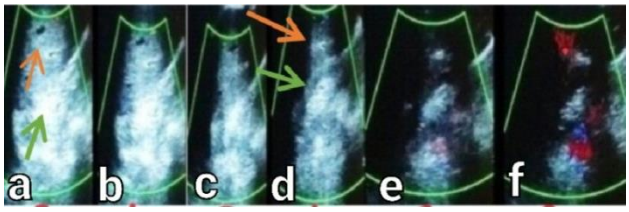

figure 6: Patient with renal failure a) reveals hyperechogenic blotches in liver (red arrow), in renal and perirenal area that covering the renal and obscured its shape (green arrow), which appears gradually through b & c, to become visible in (d) as pointing by red arrow to liver area and green arrow to renal, then color flow become visualized as shown in e & f with distinguish of renal sinus from renal cortex and liver become free of fibrosis or fatty like reflection and size of renal is increased in length and width as the fibrosis (hyperechogenic reflection) is abolished on day 21 of therapy.

7- On day 21 of therapy there is an appearance of color flow in collateral vessels that have a dark or black echogenicity before therapy.

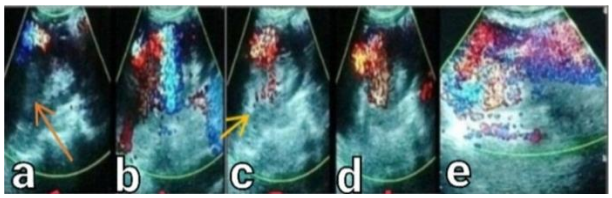

figure 7: Patient with renal failure; (a) show black or darck area with central faint echogenic (red arrow) which is the slowest collateral circulation, then it became brown in color in (b) and white central with gray periphery (orange arrow) in (c & d) while in (e) widest extension of multiple coulorized collateral vessles on day 21 of therapy.

8- Opening of contracted renal interlobar, interlobular vessels and parts of arcuate arteries with appearance of new artery (bright red) and increased in their numbers

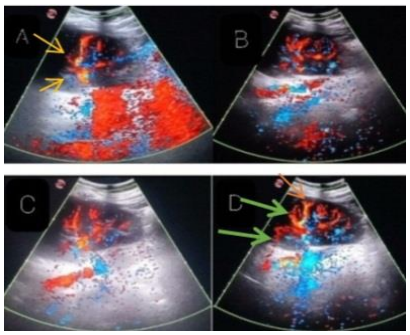

figure 8: (A) orange arrows pointing to amputated renal interlobar arteries, and middle arteries with no interlobular arteries, then the arterial is continuing to enlarged till it increased in numbers, length and width with orange arrow pointing to interlobular arteries of middle one and green arrows pointing to reopening of amputated artery (upper) and new artery (lower) in (D).

9- Improvement in renal veins with dilated of the narrowed area and increased in venous drainage, with appearance of interlobular and arcuate arteries as shown in figure 9.

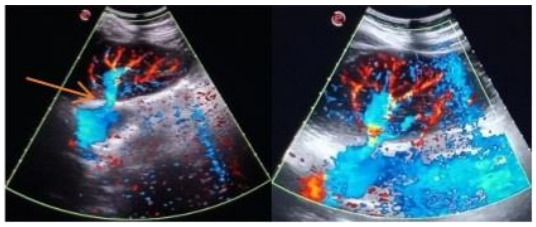

figure 9: red arrow pointing to narrowed renal vein and in other photo the main renal vein is dilated and collateral venous vessels that seen as blue network is extended largely., with more branches of interlobar arteries and reappearance of arcuate arteries.

Ultrasonography spectral doppler results:

By spectral doppler the recorded blood flow waves from segmental to interlobular revealing increase in systolic velocity and decreased in diastolic velocity, with loss of slope but after therapy the diastolic wave is increased in velocity at beginning and decreased at the end forming slope form from segmental level to cortical one.

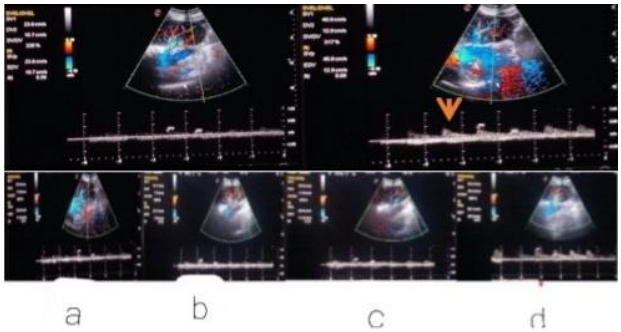

figure 10: systolic-diastolic phase changed from linear to sloping form (red arrow) at cortical levels, i.e. the vessels are retaining its elasticity which reflected by higher level of diastolic wave at beginning and lower level at end as the blood volume in distensible vessels decreased gradually before the appearance of next systolic wave. A) increased systolic velocity while diastolic is linear and low, b) diastolic start to increase but near to linear, c) then systolic tip increased, d) increased of systolic and diastolic with slop at cortical level, pointing to return of elasticity.

Drugs, medicinal herbal substances, home herbal particles and fruits effects on therapy revealing continues change with change in therapeutic regimes from time to another as shown in tables (2 – 13), and explained together by taking a samples in table (14).

Table (14) Represents a samples of changes in Drugs, Herbal Pharmaceutical Drugs and Home herbal Substances that are used in treatment of patients depends on their effects either positive or negative as

12/6/022	Clar	Amoxicillin	D3 & Ca	Clop	Ator	Eye Drops	Hot drink													
17/8/022	Clarithro	Amoxicillin	D3 & Ca	Clop	Ator	Eye Drops	Hot Drink	Vit. A & E	Aspirin											
23/8/022			D3 & Ca	Clop	Ator		Hot Drink	Vit. A & E	Aspirin	Ginkgo B.	Rumalaya F,									
3/10/022	Clarithro	Amoxicillin	D3 & Ca	Clop	Ator		Hot drink	Vit. A & E		Ginkgo B.	Rumalaya F.	SL. Cinn. F.	Azathioprin	SL powder	Hot D&SL F.	Nasal Cinn				
29/10/022	Clarithro	Amoxicillin		Clop	Simva+Ezet		Hot Drink			Ginkgo B	Rumalaya F.		Azathioprin	SL. Powder						
6/11/022	Clarithro	Amoxicillin		Clop	Ator	Eye Drops	Hot Drink	Vit. A & E		Ginkgo B.	Rumalaya F.			SL. Powder		Nasal Cinn				
26/11/022	Clarithro	Amoxicillin		Clop	Ator	Eye Drops	Hot Drink	Vit. A & E		Ginkgo B.	Rumalaya F.	Tea SL. F	Azathioprin			Nasal Cinn	Roxithromy cl	Echinacea P		

01/01/023	Clarithro	Amoxicillin	Vit. D3 & Ca	Clop	Ator	Eye Drops	Hot Drink			Ginkgo B.	Rumalaya F.	Coffee SL. D	Azathioprin	SL. Powder		Nasal Cinn		Echinacea P		
14/04/023	Clarithro	Amoxicillin	Vit. D3 & Ca	Clop	Ator		Hot Drink	Vit. A & E						SL. Powder					Septilin	
17/06/023	Clarithro	Amoxicillin		Clop	Rusovast		Hot Drink													B.Frankince
21/06/023	Clarithro	Amoxicilli		Clop	Ator		Hot Drink													B.Frankinc
25/06/023	Clarithro	Amoxicillin		Clop	Simva+Ezet		Hot Drink													B.Frankince

Laboratory investigation: Reveals improvements in renal function creatinine from 3.6 mg /dl to 1.9 mg /dl within first week & to 0.9 mg /dl in the second week, sugar and HbA1C there is improvement in HbA1c levels that elevated even with/without normal sugar level, by a decrease of 33% per week, And LFT(ALT and AST) improvement within 3 weeks.

4-2-Discussion:

This study reveals the following:

1- Possibility of treatment of renal failure due to intrarenal vascular stenosis and occlusion, also reveals the importance of therapeutic prophylaxis to decrease renal failure development or progression, and disappearance of fibrosis.
2- Colorization of slow collateral circulation means improvements in its blood flow.
3- Short time needed to know if the drug or herbal substances has a positive or negative effects to human by two things; firstly, monitoring of patients manifestations and of SpO2% and PI% in all fingers by using of fingertip pulse oximeter. Secondly; by doppler imaging of renal blood flow and comparing between pre and post therapeutic state.
4- Not only the drugs and herbal substances that leads to positive or negative effects to the human body but also the food and beverages, and if either taken hot or cold.
5- Short time of 15 to 30 minutes to reveal positive or negative effects mean that the anti-inflammatory or inflammatory process inhibition or provoking respectively, are starting on the gastric mucossa.
6- To compare this study with other studies dealing with treatment of renal failure due to intrarenal vascular stenosis or occlusion reveals its benefits and faster improvements
7- Dangerous of SARS-CoV-2 variants is in progress.

Cases of renal failure improved with the reappearance of intrarenal vessels that were previously unobservable before therapy, as shown in Figures (5, 6, and 7). The reemergence of vascular parts within 15–30 minutes post-therapy indicates that the previously non-visualized renal vessels were collapsed due to localized or global spasm, as illustrated in the "b" images of the figures. This improvement was accompanied by a reduction in blood pressure by 20/10 mmHg within 15

minutes, normalizing during the first week, along with alleviation of symptoms such as reduced flank fullness and pain, headache, and chest, back, or abdominal discomfort—all achieved without antihypertensive drugs. Renal function also improved significantly, with creatinine levels dropping from 3.6 mg/dL to 1.9 mg/dL in the first week and stabilizing at 0.9 mg/dL in the second week without diuretics.

The blood pressure reduction achieved with clopidogrel, without antihypertensive medication, aligns with findings by An X. et al., who noted that platelet inhibition by clopidogrel suppresses Ang II-induced vascular inflammation, oxidative stress, and remodeling. The effective dose is 150 mg daily (two tablets), which must be taken alongside statin therapy to prevent adverse reactions, such as chest pain. Post-COVID-19 changes in drug responses necessitate combining treatments for optimal results, as demonstrated in this study.

In other studies, revascularization was associated with complications, and medical therapy required additional antihypertensive treatment after one year, with no significant difference in serum creatinine levels between medical and surgical approaches[62]. This suggests that antihypertensive medications initially reduce blood pressure slightly but fail to sustain the effect due to cytokine and chemokine reactions triggered by inflammation. Hyperechogenic areas resembling fibrosis in the liver and kidneys disappeared, as shown in Figure (6), along with increased renal size and improved morphology compared to pre-therapy images.

Zheng Z. et al. highlighted that the activation of TGF-beta, CTGF, and MAP kinases are early profibrotic signaling events, leading to fibronectin accumulation and TGF-beta-induced fibrosis in diabetic patients. While the precise mechanism of clopidogrel's therapeutic effect on diabetic kidneys requires further study[63], Chen J. et al. demonstrated that clopidogrel inhibits renal fibrosis by preventing macrophage-to-myofibroblast transition[8]. Zheng Z. et al. also reported that clopidogrel reduces fibronectin accumulation and improves diabetes-induced renal fibrosis[63]. These findings confirm clopidogrel's anti-inflammatory effects and its ability to lower blood pressure, which further supports that hypertension results from vascular inflammation.

An X. et al. corroborated this by showing that clopidogrel suppresses Ang II-induced vascular inflammation, oxidative stress, and remodeling[64]. Another drug with antifibrotic properties is statin therapy, which inhibits TGF-beta, as stated by Dolivo D.D. et al.[65].

Table [15] highlights the key findings: reopening of stenosed intrarenal vessels (arteries and veins), reappearance of previously unseen vascular parts, fibrosis elimination, and blood pressure normalization. These benefits confirm the therapeutic potential of this regimen in treating renal failure. Sonographic evidence often reveals reduced renal arteries or absent colored vessels pre-treatment, which can lead to renal atrophy. This suggests renal vascular stenosis, caused by inflammatory processes (pro-inflammatory cytokines), is the primary event leading to hypertension and renal atrophy. Treating vascular stenosis, not hypertension alone, is essential, as hypertension is secondary. Addressing only hypertension risks latent ischemia, manifesting as flank pain or discomfort.

Monitoring was doing within 5-30 minutes using pulse oximeter and patients reported symptomes and signs like reduced pain or blood pressure and doppler imaging confirms these improvements, Substances ingested interact with gastric mucosa, producing cytokines and chemokines that affect inflammatory pathways. Quercetin, found in onions and apples, reduces IL-6 and TNF-alpha, exhibiting anti-inflammatory properties.

Table 15 highlights how pharmaceuticals and herbs modulate cytokines, crucial during COVID-19. Clopidogrel, statins, and vitamins D3, A, and E lower pro-inflammatory markers like IL-6, while amoxicillin upregulates it. Herbal substances (e.g., Ginkgo Biloba, ginger, clove, cinnamon, and cardamom) show diverse effects, such as activating the Nrf2

pathway or modulating Foxp3 expression to balance autoimmune responses. For example, clove and cinnamon decrease interferon-gamma, while ginger enhances the Nrf2 pathway's anti-inflammatory function.

This study emphasizes the need to evaluate local (mouth, gastric mucosa) and systemic effects of drugs, herbs, and dietary components on cytokines, guiding integration of herbal and conventional therapies for chronic diseases or malignancies. Healthcare providers should consider these interactions for holistic treatment approaches, particularly for COVID-19, malignancy, or renal failure patients.

Table (15) Represents the effect of Drugs, Herbal Pharmaceutical Drugs and Home herbal Substances on cytokines and chemokines

Cytokines & chemokines	*Covid-19*	*Clarithromycin*	*Amoxicillin*	*Clopidogrel*	*Atorvastatin*	*Simvastatin*	*Rosuvastati*	*Ezetimib*	*azathioprin*	*Ginkgo Biloba*	*Rumalaya Forte*	*Roxithromycin*	*Tea*	*Coffee*	*Curcum*	*Ginger*	*Clove*	*Cardamom*	*Cinnamon*
TNF-alpha	Act [1]	D [49]	UR [56]	D[5, 7]	ND	ND	I (18,	ND	S[61]	Inh[60]	DR[43] D[46]	D[49]	ND	D[37]	Pr.[2, 26]	Pr[41]	ND	D[30]	ND
TNF-beta	-	ND	ND	D[7]	ND	ND	ND	ND	ND	ND	ND	ND	D[38]	ND	ND	ND	ND	ND	ND
IFN-gamma	-	RR [51]*	ND	ND	D[10]	D(11) I[12,15]	NE[18]	ND	ND	ND	D[43] EN[48]	DR[38]	ND	NE[36]	D[26]	ND	D[33]	D[31]	D[35]
TGF-beta	-	ND	inh [56]	Pr[8, 9]	Pr[23], D[42]	I[13]	D[42]	NE	ND	ND	ND	D[40]	ND	ND	ND	ND	I[33]	ND	ND
IL-1alpha	D [53]	inh [49]	NE [56]	D[7]	ND	ND	I[18]	ND	ND	inh[60]	D[43]	inh[49]	ND	ND	Pr.[24]	ND	ND	ND	ND
IL-1beta	D[53]	D [49]	ND	ND	D[42]	ND	D[42]	DR[42]	NE[61]	inh[60]	D[43]	inh[49]	D[38]	NE[36, 37]	D[29]	Pr[41]	Pr[34]	D[31]	D[35]
IL-2	Act [1]	inh [3]	ND	[(7]	ND	ND	I[18]	ND	ND	ND	D[43], EN[48]	ND	ND	ND	ND	ND	Pr.[33]	ND	ND
IL-3	Act [52]	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
IL-4	ND	ND	ND	ND	ND	I[11, 12, 15]	I[18]	ND	ND	NDND	D(43) UR[43]	ND	ND	NE[36]	D[41]	ND	I[33]	ND	ND
IL-5	NE [1]	ND	ND	ND	ND	I[11]	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
IL-6	Act [1]	inh [3] D [49]	UR [56]	D[7, 9]	ND	D(12, 15, 16]	D(18, 1	ND	D[61]	inh[60]	D[43, 46]	Pr[49]	D[38]	I[36] NE[37]	Pr[24] D[41]	ND	Pr.[34]	D[31]	ND
IL-7	I[1]	D[49]	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
IL-8 (cxc8)	Act [1]	D [50] inh [49]	ND	D[5]	ND	ND	I[18]	ND	D[61]	inh[58]	DR[48]	inh[49]	Pr.[38]	NE[36, 37]	Pr[24, 26]	ND	ND	ND	ND
IL-10	I[1]	D[49]	UR[56]	D[7]	I[10, 42]	I[16]	D[20]	NE	ND	UR[60]	D[46]	D[49]	ND	I[36]	I[28]	I[41]	I[33] pr.[34]	ND	I[35]
IL-12	D[53]	inh[51] *	ND	ND	ND	ND	ND	ND	D[61]	ND	EN[48]	ND	ND	NE[36]	ND	ND	ND	ND	ND
IL-13	I[54]	ND	ND	D[7]	ND	I[11]	ND	ND	ND	ND	ND	ND	ND	ND	D[41]	ND	ND	ND	ND
IL-15	D[53], E[55]	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND

JNK	ERK	PDGF	P-selectin	RANTES	NF-kB	CTLA-4	TLR4	MIP-1beta	MIP-1 alpha	MCP-1 (ccl2)	VCAM-1	maturation of	ICAM-1	IL-37	IL-35	IL-27	IL-23	IL-22	IL-21	IL-20	IL-18	IL-17
-	-	-	-	NE [1]	I[75]	-	I[74]	ND	I[1]	I[1]	I[55]	ND	I [55]	ND	ND	D [53]	I[72]	I[2]	Act [1]	I[2]	E[55]	I[7]
ND	ND	ND	ND	ND	ND	UR[3]	D[3]	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	inh [51]*	ND
ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
S[9]	S[9]	ND	P[8]	UR	Pr[38]	ND	ND	UR	ND	ND	Re[9]	ND	Re[9]	ND	ND	ND	ND	ND	ND	ND	ND	D[6]
ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	I[42]	D[42]	ND	D[42]	ND	D[10]	ND	D[42]	D[10]
ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	I[12, 15]	D[12, 15, 16]	ND	D[15]	ND	ND	D[12, 15]
ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	I[18]	ND	I[42]	ND	I[42]	D[42]	ND	ND	ND	ND	ND	ND	ND
ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	NE	ND	NE	ND	ND	ND	NE	ND
ND	ND	ND	ND	ND	S[61]	ND	ND	ND	ND	D[61]	D[61]	block	NE	ND	ND	ND	ND	ND	ND	ND	ND	ND
ND	ND	ND	ND	ND	DR[57]	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	DR[60]
UR[44]	NE	ND	ND	ND	D[46]	ND	ND	ND	ND	ND	D[47]	ND	D[47]	ND	ND	ND	ND	ND	ND	ND	ND	D[45]
ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	Pr[40]	ND	ND	ND	ND	ND	ND	ND	ND	ND
ND	ND	ND	ND	ND	Pr.[38]	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
D[25]	ND	ND	ND	ND	D[25], S[41]	ND	ND	D[25]	ND	D[25]	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	D[29]	ND
ND	ND	ND	ND	ND	Pr[41]	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	Pr[41]
ND	ND	ND	ND	ND	Pr[34]	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
ND	ND	ND	ND	ND	D[32]	ND	ND	ND	ND	D[31]	D[30]	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND

SDF1 (cxcl12	*IP10 (cxcl10*	*GRO beta*	*GRO alpha*	*MMT*	*Lymphocyte*	*VEGF*	*Foxp3*	*SMAD 6 & 7*	*JAK-STAT*	*Treg supp.*	*GATA3*	*SOCS7*	*SOCS3*	*Th2*	*Th1*	*Th1/Th17*	*Diff. Th17*	*Diff. CD4*	*Treg*	*Nrf2 pathwa*	*ROS*	*MPO*
-	I [1, 52]	-	-	ND		-	DR[73]		-	-	-	-	-	-	-	-	-	-	-	-	-	-
ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	Act[9]	R[9]	D[6]
ND	ND	ND	ND	Inh[23]	D[22]	ND	I[22]	ND	ND	I[21]	ND	ND	ND	I[22]	D[22]	D[22]	ND	ND	Re(10) I[21,	ND	ND	ND
ND	ND	ND	ND	ND	ND	ND	I[13, 17]	D[17]	D[15]	I[14, 16]	I[11]	I[15]	I[12, 15]	ND	ND	ND	D[16]	I[17]	I[14, 16, 17]	ND	ND	ND
ND	ND	ND	ND	ND	ND	I[18]	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
ND	D[61]	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
ND	ND	ND	ND	ND	ND	inh[58]	I[60]	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	UR[60]	Act[59]	R[60]	ND
ND	ND	ND	ND	ND	ND	D[44]	D[45]	ND	Pr[45]	ND	ND	ND	ND	ND	ND	ND	Pr[45]	ND	ND	ND	ND	ND
ND	NE [38]	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
D[25]	D[25]	D[25]	D[25]	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	I[28]	ND	ND	ND
ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	I[41]	ND	ND
ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	Ac[32]	ND	ND
ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND

Leukotrienes	*Prostaglandin*	*HO-1*	*MPO*	*MAPK Pathwa*	*STAT*	*Arachidonic*	*Nitric Oxide*	*COX-2*	*COX-1*	*CCR4*	*TREM-1*	*STAT1/ IL-10*	*NLRP1, 3,4,5,6*	*G. peroxid*	*Nitric oxide*	*TXNIP/ NLRP3*	*P38*	*TLR2/4 /7*	*AMPK*	*MMP-9*	*MMP-3*	*MMP-2*
-	-	-	-	-	-	_	-	I[73]	-	-	-	-	-	-	-	-	-	-	-	-	-	-
ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
ND	ND	ND	ND	ND	ND	ND	ND	DR[57]	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
D[43]	Pr[43], D[46]	ND	ND	Pr[46]	ND	ND	ND	D[44] S[46]	ND	ND	ND	ND	ND	ND	ND	ND	Pr[46]	ND	ND	D[44]	ND	ND
ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	D[38]	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	D[38]	ND	ND	ND	ND	ND	ND	ND	ND	Pr[38]	Pr[38]	ND
ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	DR[37]	I[37]	ND	ND	ND	ND	ND	ND	ND	ND	ND
ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	Dre[29]	D[25]	D[25]	Ac[27]	D[25]	ND	D[25]
ND	Pr[41]	I[41]	Pr[41]	S[41]	S[41]	Pr[41]	D[41]	Pr[41]	Pr[41]	ND	ND	ND	S[41]	ND	ND	ND	ND	ND	ND	ND	ND	ND
ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	D[31]	ND	ND	ND	ND	ND	ND	ND
ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	I[35]	ND	ND	ND	ND	ND	ND	ND	ND

Eotaxin -1	-	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	DR[48]	ND	ND	ND	ND	ND	ND	ND
GM-CSF	H [53]	Inh[49]	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	inh[49]	ND	ND	ND	ND	ND	ND
G-CSF	I[1] H[53]	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
CCL3	H [52]	D[49]	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	D[49]	ND	ND	ND	ND	ND	ND
CCL5 (RANTE	H [52]	D[49]	ND	ND	ND	ND	ND	ND	ND	D[61]	ND	ND	d[49]	ND	ND	ND	ND	ND	ND
CCL20	-	D [49]	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	D[49]	ND	ND	ND	ND	ND	ND
CCL22	-	D [49]	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	D[49]	ND	ND	ND	ND	ND	ND
CXCL1	-	D [49]	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	D[49]	ND	ND	ND	ND	ND	ND
CXCL5	-	D [49]	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	D[49]	ND	ND	ND	ND	ND	ND
Rac1	-	ND	ND	ND	ND	ND	ND	ND	ND	inh[61]	ND	ND	ND	ND	ND	ND	ND	ND	ND

1-D, Decreased. DR-down regulated. UR-up regulated. Pr.-prevent or inhibited. Re –re-regulate, R. reduced. Ac-activation. S-suppressed. MMT- Macrophage to Myofibroblast Transition. NE- No Effect. ND- No Data. Inh. Inhibit. * as a conclusion result. RR- reregulate. H- high. E- Enhanced. – not needed.

Helicobacter pylori secretes substances that activating NF-kB, IL-8, IL-2, TNF-alpha, MIP-1 alpha, IL-1 beta, IL-6, IL-10, IL-12, IL-18 and IL-13[69],and from non-published study there is an provoking stimuli by SARS-CoV-2 variants to H. pylori chronic inflammatory process, that the arterial stenosis is one of its sequel, and exaggerated more in last years after viral infection. A point that explains one of the benefits of antibiotics in addition to their effects on cytokines and chemokines, in treatment of SARS-CoV-2 variants sequel.

This research demonstrates faster results, quicker symptom relief, and comprehensive inflammatory treatment across organs compared to other studies, as outlined in Table 1. Patient improvements were consistent, but the emergence of SARS-CoV-2 variants caused recurrent disease, with organ involvement varying based on drugs, herbs, or dietary substances used. Sustained use of P2Y12 antiplatelet inhibitors and statins (HM-CoA reductase inhibitors), alongside effective drugs, helps mitigate vascular issues. However, aspirin showed positive effects temporarily in 2022 but later caused ischemic symptoms, evidenced by the disappearance of collateral vessels (Figure 1, Photo B).

Bhatt et al. (2002) highlighted clopidogrel's role in improving renal function. Post-COVID-19, the combined use of clopidogrel and statins is crucial, as SARS-CoV-2 variants adapt to evade interventions and perpetuate inflammation via gastric mucosa. Chronic H. pylori inflammation and animal-to-human viral transmission exacerbate this. For example, goat blindness during active infection improved within three days with hot tea and Septilin tablets.

Treatment regimens evolved: 2020–2021 included clarithromycin, amoxicillin, ginkgo biloba, Echinacea syrup, and azathioprine. From 2022, vascular cases increased, requiring clopidogrel and atorvastatin additions. By mid-2023, physical interventions like covering the nose, mouth, or ears were explored, highlighting the complexity of achieving full recovery without addressing human-animal transmission and route-specific inflammatory triggers.

5-CONCLUSION:

1) Treatment of intrarenal vascular stenosis, renal fibrosis and renal failure is possible
2) Transforming growth factor (TGF-beta) that is responsible for fibrosis is decreased by amoxicillin, clopidogrel, atorvastatin, rosuvastatin and Roxithromycin, while simvastatin and clove are increased it, and others with no available data, is an opposite action in spite of its benefits that mandate holistic study.
3) Drugs, herbs, home herbal substances, fruits, vegetables, spicy, food and beverages all have an effect on cytokines and chemokines firstly at level of mouth and gastric within 5 to 10 minutes or less, then progress according to what enter to the gastric either of positive or negative effect.
4) Clopidogrel 150 mg, statin low dose 10 mg, are better than Aspirin 75mg, Statin 10 mg and Clopidogrel 75 mg in the period with negative effects of Aspirin.
5) Clopidogrel in a dose of two tablets together with a suitable statin drug make stenotic renal vessels re-opening and the renal function normalized, in addition to other arteries and veins.
6) Clopidogrel in a dose of two tablets considered with no danger if patients not using a Ginger or Raw Garlic during the period of treatment, and if menstruating women are stopped it about 5 - 7 days before menstruation.
7) Clopidogrel and suitable statin can treat renal failure if used together with other therapeutic regime that make positive effect in patient with decreased SpO2% and/or increased PI%.
8) Clopidogrel and suitable statin can treat Hypertension and Hypotension in a short period, if no sequel of SARS-CoV-2 variants that known by decreased of SpO2% &/or Increased of PI%.
9) Clopidogrel with/without Statin Positive effects may be changed to negative depends on the effects of SARS-CoV-2 variants mutation.
10) Therapeutic regimes may be changed according to the frequent emergence of SARS-CoV-2 variants and its effects.
11) Eradication of SARS-CoV-2 variants needs the same therapeutic program for human and surrounding Animals at the same time according to positive and negative effects of herbal and home herbal substances and same routs of administration.

COMPETING INTERESTS:

No competing interest

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Recommendation.

1. **Reduce Renal Failure Cases**: Implement measures to treat renal failure, hypertension, cardiac disease, dementia, and vascular conditions, minimizing bleeding risks by avoiding ginger, raw garlic, and discontinuing these seven days before menstruation.
2. **Comprehensive Monitoring Systems**: Develop digital or mobile apps to help patients track renal health, symptoms, medication adherence, and dietary habits, using data visualization to highlight the impact of lifestyle choices on renal function.
3. **Educational Programs**: Design patient and family-focused initiatives to promote dietary and lifestyle changes that complement treatments for renal vascular stenosis, emphasizing the role of specific foods, herbs, and medication adherence.
4. **Personalized Treatment Protocols**: Create tailored treatment plans considering genetic, lifestyle, and comorbid factors, optimizing the use of medications like Clopidogrel and statins to improve outcomes while minimizing side effects.

5. **Community Support Networks**: Establish support groups to provide emotional encouragement, share dietary and lifestyle advice, and host healthcare professionals for discussions on new research and treatment options.
6. **Suggestions for Complementary Studies**

1. **Long-Term Dietary Impact Study**: Conduct a longitudinal study to evaluate the effects of high fruit and vegetable intake and herbal supplements on renal function in patients with vascular stenosis, correlating dietary patterns with renal health improvements over time.
2. **Comparative Analysis of Antiplatelet Agents**: Design a study comparing the efficacy and safety of antiplatelet agents like Clopidogrel and Aspirin in treating renal vascular stenosis, focusing on clinical outcomes, quality of life, and medication side effects.
3. **Cytokines and Chemokines Research**: Investigate the effects of drugs, herbs, fruits, vegetables, and beverages on cytokines and chemokines at the gastric mucosa level, correlating findings with patient symptoms and changes in creatinine levels.

REFFERENCES.

1- Rokni, M., Hamblin, M. R., & Rezaei, N. (2020). Cytokines and COVID-19: Friends or foes? Human Vaccines & Immunotherapeutics, 16(10), 2363-2365. https://doi.org/10.1080/21645515.2020.1799669
2- Fang, S., Ju, D., Lin, Y., & Chen, W. (2022). The role of interleukin-22 in lung health and its therapeutic potential for COVID-19. Frontiers in Immunology, 13, 951107. https://doi.org/10.3389/fimmu.2022.951107
3- Sugiyama, K., Shirai, R., Mukae, H., Ishimoto, H., Nagata, T., Sakamoto, N., Ishii, H., Nakayama, S., Yanagihara, K., Mizuta, Y., & Kohno, S. (2007). Differing effects of clarithromycin and azithromycin on cytokine production by murine dendritic cells. Clinical and Experimental Immunology, 147(3), 540-546.
4- Ge, H., Zhou, Y., Liu, X., Nie, X., Wang, Z., Guo, Y., Chen, W., & Yang, Q. (2012). Relationship between plasma inflammatory markers and platelet aggregation in patients with clopidogrel resistance after angioplasty. Angiology, 63(1), 62-66.
5- Al-Bahrani, A., Taha, S., Shaath, H., & Bakhiet, M. (2007). TNF-alpha and IL-8 in acute stroke and the modulation of these cytokines by antiplatelet agents. Current Neurovascular Research, 4(1), 31-37.
6- Heitzer, T., Rudolph, V., Schwedhelm, E., Karstens, M., Sydow, K., Ortak, M., Tschentscher, P., Meinertz, T., Böger, R., & Baldus, S. (2006). Clopidogrel improves systemic endothelial nitric oxide bioavailability in patients with coronary artery disease: Evidence for antioxidant and anti-inflammatory effects. Arteriosclerosis, Thrombosis, and Vascular Biology, 26(7), 1648-1652.
7- Antonino, M. J., Mahla, E., Bliden, K. P., Tantry, U. S., & Gurbel, P. A. (2009). Effect of long-term clopidogrel treatment on platelet function and inflammation in patients undergoing coronary artery disease: Biomarker profile and long-term clopidogrel. American Journal of Cardiology, https://doi.org/10.1016/j.amjcard.2009.01.367
8- Chen, J., Tang, Y., Zhong, Y., Wei, B., Huang, X. R., Ming, P., Tang, K., Xu, A., & Lan, H. (2022). P2Y12 inhibitor clopidogrel inhibits renal fibrosis by blocking macrophage to myofibroblast transition. Molecular Therapy, 30(9), 2074-2087.
9- Li, B., Zhang, Y., Zheng, Y., & Cai, H. (2024). The mechanisms and therapeutic potential of clopidogrel in mitigating diabetic cardiomyopathy in db/db mice. iScience, 27, 109134. https://doi.org/10.1016/j.isci.2024.109134
10- Eller, P., Eller, K., Wolf, A. M., & Oberhuber, G. (2010). Atorvastatin attenuates murine anti-glomerular basement membrane glomerulonephritis. Kidney International, 77(5), 428-435.
11- Arora, M., Chen, L., Paglia, M., Gallagher, A., Allen, M., & Manickam, M. (2006). Simvastatin promotes Th2-type responses through the induction of the chitinase family member Ym1 in dendritic cells. Proceedings of the National Academy of Sciences of the United States of America, 103(20), 7777-7782.
12- Zhang, X., Jin, J., Peng, X., Ramgolam, V. S., & Markovic-Plese, S. (2008). Simvastatin inhibits IL-17 secretion by targeting multiple IL-17 regulatory cytokines and by inhibiting the expression of IL-17 transcription factor RORC in CD4+ lymphocytes. Journal of Immunology, 180(10), 6988-6996.
13- Lee, K. J., Moon, J. Y., Choi, H. K., Kim, K. K., & Lee, S. H. (2010). Immune regulatory effects of simvastatin on regulatory T cell-mediated tumour immune tolerance. Clinical and Experimental Immunology, 161(2), 298-305.
14- Meng, X., Zhang, K., Li, J., Dong, X., Meng, J., Zhao, X., & Li, Y. (2012). Statins induce the accumulation of regulatory T cells in atherosclerotic plaque. Molecular Medicine, 18(4), 598-605.

15- Chamani, S., Kooshkaki, O., Moossavi, M., Rastegar, M., Soflaei, S. S., McCloskey, A. P., Banach, M., & Sahebkar, A. (2023). The effects of statins on the function and differentiation of blood cells. Archives of Medical Science, 19(5), 1314-1326. https://doi.org/10.5114/aoms/158546

16- Maneechotesuwan, K., Kasetsinsombat, K., Wamanuttajinda, V., Wongkajornsilp, A., & Barnes, P. J. (2013). Statins enhance the effects of corticosteroids on the balance between regulatory T cells and Th17 cells. Clinical & Experimental Allergy, 43(2), 212-222.

17- Kim, Y. C., Kim, K. K., & Shevach, E. M. (2010). Simvastatin induces Foxp3+ T regulatory cells by modulation of transforming growth factor-beta signal transduction. Immunology, 130(4), 484-493. https://doi.org/10.1111/j.1365-2567.2010.03398.x

18- Vavlukis, A., Vavlukis, M., Dimovski, A., Petrushevska, G., Eftimov, A., Domazetovska, S., & Mladenovska, K. (2022). Anti-inflammatory and immunomodulatory effects of rosuvastatin in patients with low to moderate cardiovascular risk. Acta Pharmaceutica, 72(3), 303-315. https://doi.org/10.2478/acph-2022-0018

19- Andrianto, A., A'Yun, M. Q., Suryawan, I. R., & Triastuti, F. (2024). Rosuvastatin administration and its effect on IL-6, IL-1β, and TNF-α cytokine levels in peripheral blood mononuclear cells of type II diabetes mellitus patients with COVID-19. Modern Medicine, 31(1), 27-35. https://doi.org/10.31689/rmm.2024.31.1.27

20- Aguilar, M. S., Perez, H. T., Sanchez, J. J., Rios, J. M. V., Perez, P. M., Mendoza, E. C., Reyna, M. S., Corzo, J. G. T., & Moscoso, A. G. (2013). Effect of rosuvastatin on cytokines after traumatic head injury. Journal of Neurosurgery. https://doi.org/10.3171/2012.12.JNS121084

21- Mausner-Fainberg, K., Luboshits, G., Mor, A., Berrebi, A., & Nussbaum, G. (2008). The effect of HMG-CoA reductase inhibitors on naturally occurring CD4+CD25+ T cells. Atherosclerosis, 197(2), 829-839. https://doi.org/10.1016/j.atherosclerosis.2007.09.007

22- Li, X. L., Liu, Y., Cao, L. L., Zhang, P., Yan, W. X., Shen, H. H., & Zuo, Z. X. (2013). Atorvastatin modified dendritic cells in vitro ameliorate experimental autoimmune myasthenia gravis by up-regulated Treg cells and shifted Th1/Th17 to Th2 cytokines. Molecular and Cellular Neuroscience, 56(1), 85-95. https://doi.org/10.1016/j.mcn.2013.03.003

23- Chen, J., Tang, Y., Zhong, Y., Wei, B., Huang, X. R., Tang, P. M. K., Xu, A., & Lan, H. Y. (2022). P2Y12 inhibitor clopidogrel inhibits renal fibrosis by blocking macrophage to myofibroblast transition. Molecular Therapy, 30(9), 2831-2845. https://doi.org/10.1016/j.ymthe.2022.06.019

24- Zhang, B., Swamy, S., Balijepalli, S., Panicker, S., Mooliyil, J., Sherman, M. A., Skare, P., Sui, J., & Wang, T. T. (2019). Direct pulmonary delivery of solubilized curcumin reduces severity of lethal pneumonia. FASEB Journal, 33(12), 13294-13309. https://doi.org/10.1096/fj.201901047RR

25- Dai, J., Gu, L., Su, Y., Wang, Q., Zhao, Y., Chen, X., Zhou, W., & Tang, Q. (2018). Inhibition of curcumin on influenza A virus infection and influenza pneumonia via oxidative stress, TLR2/4, p38/JNK MAPK, and NF-kB pathways. International Immunopharmacology, 54, 177-187. https://doi.org/10.1016/j.intimp.2017.11.009

26- Kim, S. G., Veena, M. S., Basak, S. K., Han, E., Tajima, T., Gjertson, D. W., & Meyskens, F. L. (2011). Curcumin treatment suppresses IKK beta kinase activity of salivary cells of patients with head and neck cancer: A pilot study. Clinical Cancer Research, 17(19), 5953-5961. https://doi.org/10.1158/1078-0432.CCR-11-1272

27- Han, S., Xu, J., Guo, X., & Huang, M. (2018). Curcumin ameliorates severe influenza pneumonia via attenuating lung injury and regulating macrophage cytokines production. Clinical and Experimental Pharmacology and Physiology, 45(1), 84-93. https://doi.org/10.1111/1440-1681.12848

28- Chai, Y. S., Chen, Y. Q., Lin, S. H., Xie, K., Wang, C. J., Yang, Y. Z., & Zheng, F. L. (2020). Curcumin regulates differentiation of naive CD4+ T cells and activates IL-10 immune modulation against acute lung injury in mice. Biomedicine & Pharmacotherapy, 125, 109946. https://doi.org/10.1016/j.biopha.2020.109946

29- Ren, Y., Yang, Z., Sun, Z., Zhang, W., Chen, X., & Nie, S. (2019). Curcumin relieves paraquat-induced lung injury through inhibiting the thioredoxin interacting protein/NLR pyrin domain containing 3-mediated inflammatory pathway. Molecular Medicine Reports, 20(6), 5032-5040. https://doi.org/10.3892/mmr.2019.10742

30- Gupta, K., & Pal, N. (2021). Cardamom: the queen of spices. World Journal of Pharmaceutical and Life Science, 7(8), 147-152.

31- Heimesaat, M. M., Mousavi, S., Weschka, D., & Bereswill, S. (2021). Anti-pathogenic and immune-modulatory effects of peroral treatment with cardamom essential oil in acute murine campylobacteriosis. Microorganisms, 9(1), 169. https://doi.org/10.3390/microorganisms9010169

32- Qiblawi, S., Kausar, M. A., Shahid, S. M. A., Saeed, M., & Alazzeh, A. Y. (2020). Therapeutic intervention of cardamom in cancer and other human diseases. Journal of Pharmaceutical Research International, 32(22), 74-84. https://doi.org/10.9734/JPRI/2020/v32i2230774

33- Dibazar, S. P., Fateh, S., & Daneshmandi, S. (2014). Clove (Syzygium aromaticum) ingredients affect lymphocyte subtypes expansion and cytokine profile responses: An in vitro evaluation. Journal of Food and Drug Analysis, 22(4), 448-454. https://doi.org/10.1016/j.jfda.2014.04.005

34- Bachiege, T. F., Sousa, J. P. B., Bastos, J. K., & Sforcin, J. M. (2012). Clove and eugenol in noncytotoxic concentrations exert immunomodulatory/anti-inflammatory action on cytokine production by murine macrophages. Journal of Pharmacy and Pharmacology, 64(5), 610-616. https://doi.org/10.1111/j.2042-7158.2011.01440.x

35- Jimoh, O. A., Ayodele, A. D., Ojo, O. A., Okin-Aminu, H. O., & Olarotimi, O. J. (2024). Effects of turmeric, ginger, cinnamon, and garlic essential oils on HSP70, NF-kB, oxidative DNA damage, inflammatory cytokines, and oxidative markers in broiler chickens. Translational Animal Science, 8, txae127. https://doi.org/10.1093/tas/txae127

36- Rodas, L., Martinez, S., Aguilo, A., & Tauler, P. (2020). Caffeine supplementation induces higher IL-6 and IL-10 plasma levels in response to a treadmill exercise test. Journal of the International Society of Sports Nutrition. https://doi.org/10.1186/s12970-020-00375-4

37- Kovacs, E. G., Alatshan, A., Budai, M. M., Czimmerer, Z., Biro, E., & Benko, S. (2021). Caffeine has different immunomodulatory effects on the cytokine expression and NLRP3 inflammasome function in various human macrophage subpopulations. Nutrients, 13(7), 2409. https://doi.org/10.3390/nu13072409

38- Kobayashi, M., Shimauchi, T., Hino, R., & Tokura, Y. (2004). Roxithromycin down regulates Th2 chemokine production by keratinocytes and chemokine receptor expression on Th2 cells: Its dual inhibitory effects on ligands and the receptors. Cellular Immunology, 228(1), 27-33. https://doi.org/10.1016/j.cellimm.2004.03.011

39- Kawasaki, S., Takizawa, H., Ohtoshi, T., Takeuchi, N., Kohyama, T., Nakamura, H., Kasama, T., Kobayashi, K., Nakahara, K., Morita, Y., & Yamamoto, K. (1998). Roxithromycin inhibits cytokine production by neutrophil attachment to human bronchial epithelial cells in vitro. Antimicrobial Agents and Chemotherapy, 42(6), 1499-1502.

40- Zimmermann, P., Ziesenitz, V., Curtis, N., & Ritz, N. (2018). The immunomodulatory effects of macrolides: A systematic review of the underlying mechanisms. Frontiers in Immunology, 9, 302. https://doi.org/10.3389/fimmu.2018.00302

41- Ballester, P., Cerda, B., Arcusa, R., Marhuenda, J., Yamedjeu, K., & Zafrilla, P. (2022). Effect of ginger on inflammatory diseases. Molecules, 27(7223). https://doi.org/10.3390/molecules27217223

42- Wozniak, E., Broncel, M., Niedzielski, M., Wozniak, A., & Pabis, P. G. (2023). The effect of lipid lowering therapies on the proinflammatory and anti-inflammatory properties of vascular endothelial cells. PLOS ONE, 18(2), e0280741. https://doi.org/10.1371/journal.pone.0280741

43- Ammon, H. P. T. (2011). Erratum to "Modulation of the immune system by Boswellia Serrata extracts and boswellic acids". Phytomedicine, 18(4), 334. https://doi.org/10.1016/j.phymed.2011.01.009

44- Kunnumakkara, A. B., Banik, K., Bordoloi, D., Harsha, C., Choudhary, Sailo, B. L., Padmavathi, G., Roy, N. K., Gupta, S. C., & Aggarwal, B. B. (2018). Googling the Guggul (Commiphora and Boswellia) for prevention of chronic diseases. Frontiers in Pharmacology, 9(686). https://doi.org/10.3389/fphar.2018.00686

45- Nandan, A., Sharma, V., Banerjee, P., Sadasivam, K., Venkatesan, S., & Prasher, B. (2022). Deciphering the mechanism of Tinospora Cordifolia extract on Th17 cells through in depth transcription profiling and in silico analysis. Frontiers in Pharmacology, 13(1056677). https://doi.org/10.3389/fphar.2022.1056677

46- Hwalee, H., Ahn, E. K., Hong, S. S., & Oh, J. S. (2017). Anti-inflammatory effects of Tribulusamide D isolated from Tribulus terrestris in lipopolysaccharide-stimulated RAW264.7 macrophages. Molecular Medicine Reports, 16, 4421–4428. https://doi.org/10.3892/mmr.2017.7208

47- Fard, E. A., Fereydouni, Z., Mansouri, K., & Mostafa, A. (2020). Effect of Tribulus terrestris L. on expression of ICAM-1, VCAM-1, E-Selectin and proteome profile of human endothelial cells in vitro. Iranian Journal of Immunology, 17(1), 64–67. https://doi.org/10.22034/iji.2020.80295

48- Matsui, S., Matsumoto, H., Sonoda, Y., Ando, K., Yokota, E. A., Sato, T., & Kasahara, T. (2004). Glycyrrhizin and related compounds down-regulate production of inflammatory chemokines IL-8 and exotoxin 1 in a human lung fibroblast cell line. International Immunopharmacology, 4(1633–1644). https://doi.org/10.1016/j.intimp.2004.07.023

49- Marjanovic, N., Bosnar, M., Michielin, F., Wille, D. R., Anic-Milic, T., Culic, O., Popovic-Grle, S., Bogdan, M., Parnham, M. J., & Haber, V. E. (2011). Macrolide antibiotics broadly and distinctively inhibit cytokine and chemokine production by COPD sputum cells in vitro. Pharmacological Research, 63(5), 389–397. https://doi.org/10.1016/j.phrs.2011.02.001

50- Kovaleva, A. A., Remmelts, H. H. F., Rijkers, G. T., Hoepelman, A. I. M., Biesma, D. H., & Oosterheert, J. J. (2012). Immunomodulatory effects of macrolids during community-acquired pneumonia: A literature review. Journal of Antimicrobial Chemotherapy, 67(350–540). https://doi.org/10.1093/jac/dkr520

51- Al-Ashwal, N. S. (2021). Medicinal herbs and manufactured drugs: For treatment of COVID-19 and its complications in Aden-Yemen. Journal of Medical & Pharmaceutical Sciences, 5(1), 1–28. https://doi.org/10.26389/AJSRP.S091220

52- Channappanavar, R., & Perlman, S. (Eds.). (2017). Pathogenic human coronavirus infections: Causes and consequences of cytokine storm and immunopathology. In Seminars in immunopathology (pp. 1–15). Springer.

53- Monserrat, J., Gomez-Lahoz, A. G., Ortega, M. A., Sanz, J., Munoz, B., Arevalo-Serrano, J., Rodriguez, J. M., Gasalla, J. M., Gasulla, O., & Arranz, A. (2022). Role of innate and adaptive cytokines in the survival of COVID-19 patients. International Journal of Molecular Sciences, 23(10344). https://doi.org/10.3390/ijms231810344

54- Donlan, A. N., Sutherland, T. E., Maria, C., Preissner, S., Bradley, B. T., Carpenter, R. M., et al. (2021). IL-13 is a driver of COVID-19 severity. JCI Insight, 6(15), e150107. https://doi.org/10.1172/jci.insight.150107

55- Shaw, J. A., Meiring, M., Snyders, C., Everson, F., Sigwadhi, L. N., Ngah, V., Tromp, G., & Allwood, B., et al. (2023). Immunologic and vascular biomarkers of mortality in critical COVID-19 in a South African cohort. Frontiers in Immunology, 14(1219097). https://doi.org/10.3389/fimmu.2023.1219097

56- Melhus, A. (2001). Effects of amoxicillin on the expression of cytokines during experimental acute otitis media caused by non-typeable Haemophilus influenzae. Journal of Antimicrobial Chemotherapy, 48(3), 397–402. https://doi.org/10.1093/jac/48.3.397

57- Zou, X., Liu, S., Zou, H., Zhou, W., Fu, H., Wei, J., Zhang, J., Zeng, H., Tan, T., Zhou, W., Wu, H., Chen, X., Zhou, X. (2023). Inflammatory mechanisms of Gingko Biloba extract in improving memory functions through lncRNA-COX2/NF-kB pathway in mice with status epilepticus. CNS Neuroscience & Therapeutics, 29(471–482). https://doi.org/10.1111/cns.14019

58- Trompezinski, S., Bonneville, M., Pernet, I., Denis, A., Schmitt, D., & Viac, J. (2010). Ginkgo Biloba extract reduces VEGF and CXCL-8/IL-8 levels in keratinocytes with cumulative effect with epigallocatechin-3-gallate. Archives of Dermatological Research, 302(183–189). https://doi.org/10.1007/s00403-009-0979-x

59- Li, Y., Zhu, X., Wang, K., Zhu, L., Murray, M., & Zhou, F. (2022). The potential of Ginkgo Biloba in the treatment of human diseases and the relationship to Nrf2-mediated antioxidant protection. Journal of Pharmacy and Pharmacology, 74(1689–1699). https://doi.org/10.1093/jpp/rgac036

60- Achete de Souza, G., Vaz de Marqui, S., Matias, J. N., Guiguer, E. L., & Barbalho, S. M. (2020). Effects of Ginkgo Biloba on diseases related to oxidative stress. Planta Medica, 86(376–386). https://doi.org/10.1055/a-1109-3405

61- Marinkovic, G., Hoogenboezem, M., Hoeben, K. A., Ruiter, M. S., Kurakula, K., Rubio, I. O., Vos, M., De Vries, C. J. M., Van Buul, J. D., & De Waard, V. (2014). Inhibition of GTPase Rac1 in endothelium by 6-Merc

62- Jha, V. (2010). Should revascularization be recommended for atherosclerotic renal artery stenosis? J R Coll Physician Edinb, 40(1), 37-38. https://doi.org/10.4997/JRCPE.2010.109

63- Zheng, Z., Ma, T., Lian, X., Gao, J., Wang, W., Weng, W., Lu, X., Sun, W., Cheng, Y., Fu, Y., Rane, M. J., Gozal, E., & Cai, L. (2019). Clopidogrel reduces fibronectin accumulation and improves diabetes-induced renal fibrosis. International Journal of Biological Sciences, 15(1), 239-252. https://doi.org/10.7150/ijbs.29063

64- An, X., Jiang, G., Cheng, C., Lv, Z., Liu, Y., & Wang, F. (2018). Inhibition of platelets by clopidogrel suppressed Ang II-induced vascular inflammation, oxidative stress, and remodeling. Journal of the American Heart Association, 7, e009600. https://doi.org/10.1161/JAHA.118.009600

65- Dolivo, D. M., Reed, C. R., Gargiulo, K. A., Rodrigues, A. E., Galiano, R. D., Mustoe, T. A., & Hong, S. J. (2023). Anti-fibrotic effects of statin drugs: A review of evidence and mechanisms. Biochemical Pharmacology, 214, 115644. https://doi.org/10.1016/j.bcp.2023.115644

66- Al-Ashwal, N. S. M. (2024). Examination of renal vessels by doppler ultrasound to see renal & peri-renal vascular features in patients with or without renal disease. Journal of the Arabian Peninsula Center for Medical and Applied Researches, 1(2), 23-41. https://doi.org/10.56793/pcra23122

67- Quercetin-uses, side effects, and more. (2024, December 10). WebMD. Retrieved from www.webmd.com

68- Mueller, M., Hobiger, S., & Jungbauer, A. (2010). Anti-inflammatory activity of extracts from fruits, herbs and spices. Food Chemistry, 122(4), 987-996. https://doi.org/10.1016/j.foodchem.2010.03.041

69- Figueiredo, C. A., Marques, C. R., Costa, R. dos S., da Saliva, H. B. F., & Alcantra-Neves, N. M. (2014). Cytokines, cytokine gene polymorphisms and Helicobacter pylori infection: Friend or foe? World Journal of Gastroenterology, 20(18), 5235-5243. https://doi.org/10.3748/wjg.v20.i18.5235

70- Bhatt, D. L., Marso, S. P., & Others. (2002). Amplified benefit of clopidogrel versus aspirin in patients with diabetes mellitus. The American Journal of Cardiology, 90(6), 625-628

71- Al-Ashwal, N. S. (2021). Medicinal herbs and manufactured drugs: For treatment of COVID-19 and its complications in Aden – Yemen. Journal of Medical & Pharmaceutical Sciences, 5(1), 1-28. https://doi.org/10.26389/AJSRP.S091220

72- Smail S. W., Babaei E., Kawa A., Abdulahad W. H. (2023) Serum IL-23, IL-10, and TNF-alpha predict in hospital mortality in covid-19 patients. Front. Immunol. 14:1145840. https://doi.org/10.3389/fimmu.2023.1145840

73- Abdelhafiz A. S., Fouad M. A., Sayed-Ahmed M. M., Kamel M. M., Ali A., Fouda M., Khalil M. A., Abdel-Moneim A. S., Kamal L. M. (2021) Up-regulation of FOXP3 is associated with severity of hypoxia and poor outcomes in COVID-19 patients. Virology 563; 74-81. https://doi.org/10.1016/j.virol.2021.08.012

74- Khanmohammadi S., Rezaei N. (2021) Role of Toll-like receptors in the pathogenesis of COVID-19. J med Virol. 93: 2735-2739. https://doi.org/10.1002/jmv.26826

75- Zhou Q., Zhang L., Dong Y., Wang Y., Zhang B., Zhou S., Huang Q., Wu T., Chen G. (2024) The role of SARS-CoV-2-mediated NF-kB activation in COVID-19 patients. Hypertension Research 47: 375-384. https://doi.org/10.1038/s41440-023-01460-2