Cardiology and Cardiovascular Research
2017; 1(4): 104-112
http://www.sciencepublishinggroup.com/j/ccr
doi: 10.11648/j.ccr.20170104.12

Intrusion of Herbal Antilipidemics – Cardiac Protective Through Electromagnetic Thermal Device Patches

Rakesh Das[1, *], Sudhanshu Chakraborty[2]

[1]Department of Pharmaceutical Technology, Jadavpur University, Jadavpur, Kolkata, India

[2]School of Medical Sc. & Technology, Indian Institute of Technology (Kharagpur), Kharagpur, India

Email address:

drakesh.jupharmtech@hotmail.com (R. Das)

[*]Corresponding author

To cite this article:

Rakesh Das, Sudhanshu Chakraborty. Intrusion of Herbal Antilipidemics – Cardiac Protective Through Electromagnetic Thermal Device Patches. *Cardiology and Cardiovascular Research*. Vol. 1, No. 4, 2017, pp. 104-112. doi: 10.11648/j.ccr.20170104.12

Received: September 30, 2017; **Accepted**: October 17, 2017; **Published**: November 23, 2017

Abstract: Objective: Development of an innovated, economic and simple herbal formulation as cardiac protective through designed electromagnetic thermal device patches which induced the drugs directly to coronary arteries. This opens the blocked vessels even between 50-80% without Coronary artery bypass grafting (CABG). Material & Methods: The electromagnetic thermal device is designed with polysiloxane adhesive tape, centrally mounted with PVC membrane and over that consists of drug reservoir and in top embedded with electromagnetic vibrator. Drug use to be injected with micro-syringe and patch is operated with remote control. So, the generated heat and vibration penetrates the drug (Allicin & Arjuna) directly, vertically to coronary arteries (CA) under pericardium membrane, stored in pericardium fluid. Finally a high concentration of drugs opens the lipid choked in CA. Result & Discussion: Before and after cardiac patch drug delivery therapy ECG report, TMT, Doppler test, Angiogram analysis with the help of graphics and images, has been carried-out to evaluate the % of blockage opened. The comparative study of opening of vascular blockage through this new mechanics against other conventional drugs and CABG which proves its superior valuation. Due to herbal nature of drug contents and without any mechanical invasion, it has no adverse effects and drug interaction. Conclusion: The new innovated designed cardiac patches open the coronary artery blockage in very simply, economically, without medication error, without side effects due to herbal origin and treatment without surgery. This concludes globally emergence of the first time innovated cardiac patches convenience to patient world in medical science.

Keywords: Electromagnetic Cardiac Patch, Atherosclerosis, Coronary Artery Blockage, Non-Invasive Therapy, Innovative Intrusion of Cardiac Drugs

1. Introduction

Atherosclerosis is diseased condition which is much prone in male patients over the age of 40 years. This disease may lead to the reason of Cardiovascular Bypass Grafting (CABG) i.e., operation based on the clarification of the coagulants in coronary arteries. The 50% or less than that coagulation can be cleared by medicines, but between 50-75% obstructions is difficult to dissolve through any antiplatelet or systemic anticoagulants and antilipidaemics. For that condition, without delay surgeon's first choice is CABG. the outcomes of CABG have historically been measured in terms of mortality and morbidity; however, it has now been well recognized that adjustment to CABG is a multidimensional phenomenon that is not fully explained by medical factors [1]. Using multi arterial coronary artery bypass graft (MA-CABG), single-arterial CABG (SA-CABG) compared with percutaneous coronary intervention (PCI) using either bare metal stents (BMS) or drug-eluting stents (DES) from 1994 to 2009. It was discovered that BMS-PCI was associated with worse survival than SA-CABG, especially from 0 to 7 years ($p < 0.015$) and to a greater extent than MA-CABG was (9-year follow up: 76.3% vs. 86.9%; $p < 0.001$) [2-6]. Coronary artery bypass graft surgery (CABG) remains the most common operation performed by cardiac surgeons today. From its infancy in the 1950s till today, CABG has undergone many developments both technically and clinically. Improvements in intraoperative technique and

perioperative care have led to CABG being offered to amore broad patient profile with less complications and adverse events [7].

Due to high cost of CABG for poor as well as middle class patient, an intermediate treatment is in demand which should be economic as well as non-invasive. The conventional oral dosage forms have significant setbacks of poor bioavailability due to hepatic first pass metabolism. To improve characters of transdermal drug delivery system (TDDS) was emerged, which will improve the therapeutic efficacy and safety of drugs by specific sites within the body, thereby reducing both the size and number of doses [8]. Transdermal cardiac Patches was planned designed after getting idea of permeation enhancement effect of eugenol [9-12]. Drug Delivery Systems Division, makes the case for micro needles as a potentially transformative drug delivery system, with applications across a variety of therapeutic areas and in multiple types of drug molecule [13]. With the advent of micro-electro mechanical systems (MEMS), the field of transdermal drug delivery has seen the emergence of new technologies to bypass the skin's protective barriers [14-22]. In 2004, Mattioli Engineering introduced a new concept in dermatology for the transdermal delivery of high-molecular-weight therapeutics up to 1, 000 kDa. The Dermo electroporation (DEP) system delivers controlled current pulses between two adjacent electrodes to increase the permeability of the skin. The effect of the electrical pulses is the opening of water-based micro channels through *stratum corneum* and epidermis [23-30].

2. Material and Methods

2.1. Material Required

Adhesive tapes, polymeric membrane, electro-magnetic inductive thermal device, metered remote dose regulator, vibrators, reservoir, micro syringe, drugs (Active constituents- Allicin, Arjunosides /Terminalia Arjuna water extracts (TA aqE), preservatives, base, humidifiers etc), ECG machine, sphygmomanometers, spyrometers.

2.2. Study Design

Development of an electro-magnetic- Thermal patch with herbal constituents and its clinical effects on Cardio-vascular patients.

2.3. Designing of the Thermal Patch

The main active drug component is to be stored into the reservoir along with preservatives, eugenol base, humidifiers. The basement membrane of the patch is consisting of poly vinyl Chloride (PVC) liner polymer matrix which are located in direct contact with skin surface. And the patches would be fixed to the skin surface with water proof adhesive (polysiloxane) tape. The adjacent upper side of the reservoirs should be frame with electro-magnet, battery and mini vibrator. Additionally, a metered micro-syringe is associated to fill the moistened drugs into the reservoirs time-to-time according to the doses.

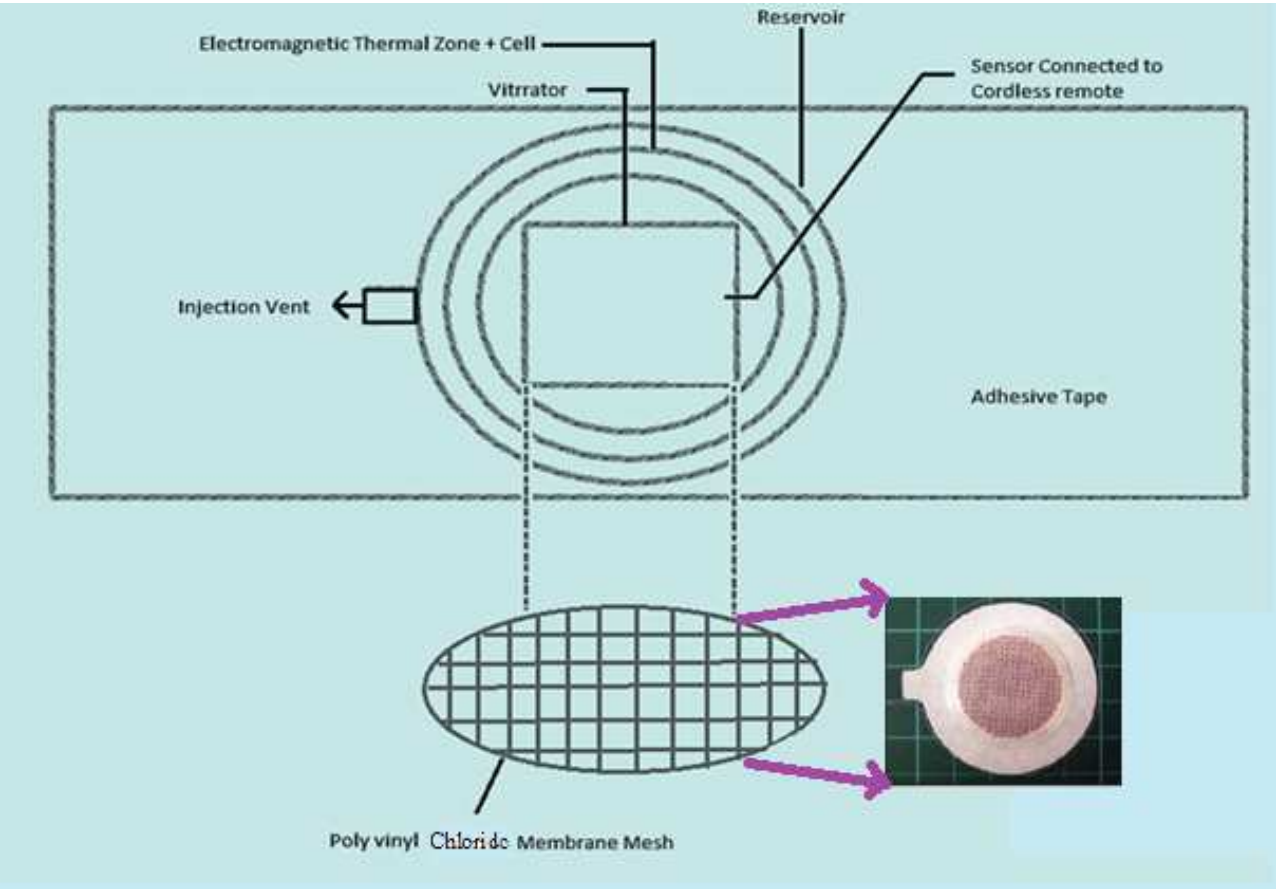

Figure 1. *Electro-magnetic pulse patch design for Cardiac patients for opening coronary opening without CABG.*

Figure 2. *Four views of Cardiac patches.*

2.4. Operating Procedures

1. The active drug Allicin is extracted through distillation process with soxhlet apparatus along with the solvent of alcohol in a regulated temperature between 40-45°C and has to be concentrated in room temperature.
2. The main active drugs are Allicin [31] and TA aqE along with the bases, natural preservatives, & humidifiers are filled into the reservoir.
3. The lower end diameter is extended as a rim down towards the skin surface to grip the chest skin. So, that the moistened drug coming out from the reservoir through the membrane resisted to displace outside the focused area.
4. The upper side of the reservoir is embedded with round electro-magnetic thermal inducted heater fixed with battery. So, that the heater warms slowly in a regulated temp. guided by remote controller from a distance. Principle of this parts of the device influx the moistened drugs vertically downward towards the skin layers due to warm surface.
5. Also, a small vibrator is located on the topmost portion of the patch. As due to high elevated distance of the vibrator from the surface of the skin, the vibration increases with the pulse response. Thus, the drugs get facilitates downwards the skins and visceral tissue with high frequency to reach up to the Pericardium [31]. The pericardial space may potentially serve as a drug delivery reservoir that might be used to deliver therapeutic substances to the heart [32-33].
6. The first dose requirements for the penetration needs much quantity, but after reaching to the pericardium rest of the doses follows the same channel slowly and low in doses. Thus, the next dose quantity would require in less amount.
7. After 2-3 dose the drugs gets accumulate over the pericardium and thus diffuse slowly into the pericardium through the pericardial fluid and thus the high concentration of drugs entered to the pericardium displace entire heart surface quickly dissolving into the pericardium fluid homogenously.
8. After that, from the surface of the heart the active constituents of Allicin and TA aqE get absorbs superficially to the coronary arteries and thus facilitates its activities.

2.5. Working Principle

The active drugs enter into the skin layers crossing the membrane. The thermal activated induction electro-magnet cum high potential difference and the vibrators influx the active constituents vertically with gravitational action through warming drug menstrum and massaging characteristics respectively. And, thus the large accumulated drugs content over the pericardium diffuses to the membrane and enters the coronary arteries. Finally, on one end the Allicin shows the Anti-lipidemics, arthrosclerosis and antiplatelate effects; and in

other end digitoxin in actively increases the inotropic activity which simultaneously increases the blood flow. Therefore, this both (Allicin+ TA aqE) active contents acts synergistically to remove the blood blockage forcefully.

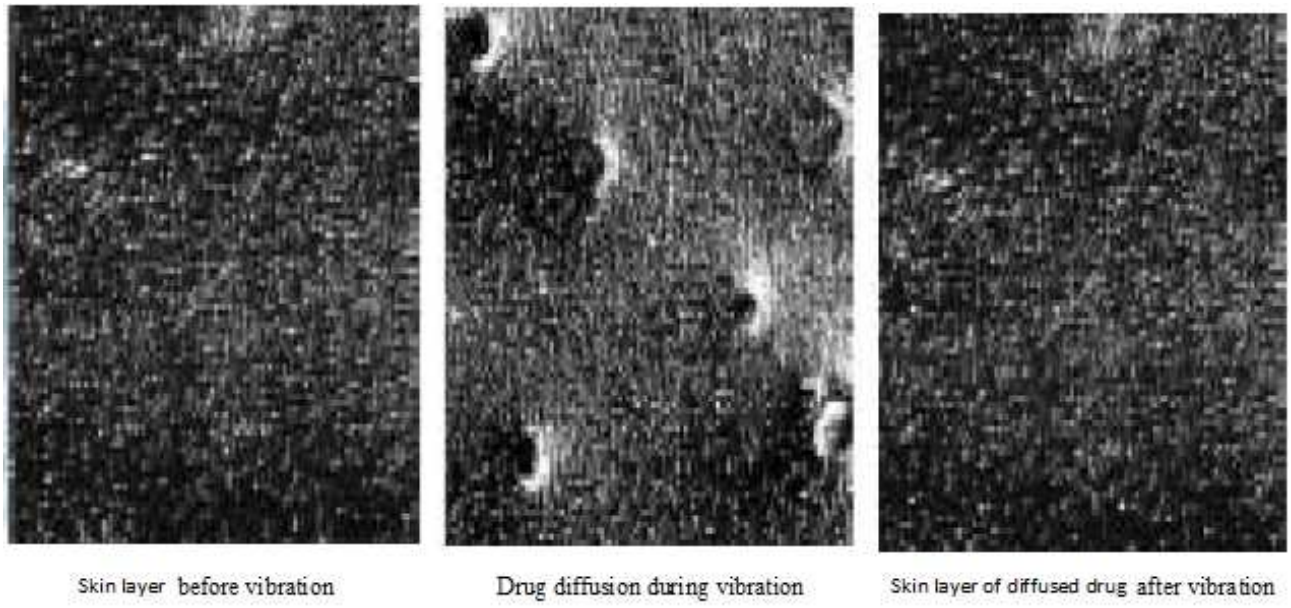

Figure 3. *Scanning Electron Microscope (SEM) detection of drug diffusion state on skin layers.*

After going through the SEM detection study of drug diffusion on skin layer in-vitro mice it is confirm that the formulated drugs could able to penetrate from the top of chest skin upto the depth of thoracic cavity (cardiac notch) bypassing the circulatory system. This drug formulation cannot get chance to enter in circulatory system (to vascular network) due to high vibratory frequency and temperature it penetrates faster in skin tissues in single vector without displacement and dispersion to peripheral tissue.

2.6. Clinical Point of View

2.6.1. Sample size

Total 40 patients have been targeted out of that 50% is healthy volunteers & 50% is Cardiac patients.

2.6.2. Sampling Technics

Only healthy and Cardio vascular patients under the acute / chronic CVD therapy is to be selected. The sampling technique is very simple, just categorizing the healthy volunteers and CVD patients separately. Then follow-up of the respiratory discomforts; ECG; working inability; intensity of other related therapeutic drugs, doses & time interval and cure duration ratio; after and before any ongoing cardiovascular drugs. The prepared Electro-magnetic-Thermal patches would be fixed to all healthy and patients volunteers and BP, ECG, TMT and Doppler test is be carried out in different time intervals.

2.6.3. Data Collection Procedure

1. Demographic data from all patients were documented and studied.
2. The lipid profile reports, TMT reports, Doppler test reports and ECG reports was collected from those patients who has gone through the above said Cardiovascular drug therapies and/or before any drug therapy.
3. The formulated dosage patches was fixed to the patient's chest and again the same above test was repeated & reported.
4. The reporting datas were interpreted and compared to get the intensity of the invented device (patches).
5. Also data of respiratory rate and capacity and congestion activity was evaluated after and before using of this device.
6. Datas for identification of skin allergy scrutinized and which shows no allergic reports till now.
7. Also datas of any types of Drug Interaction should be evaluated.

3. Result and Discussion

Patients selected for the clinical investigation on their will-full interest signed patient consent form along with interest from the patient party because it is a non-invasive and free from drug interaction (bypassing systemic circulation & herbal content). For the investigation, patients have gone through Electro-cardiogram (ECG), Tread Mill Test (TMT), Doppler test, Angiogram and Spyrometric test.

3.1. ECG Assessment

The ECG reports before treatment of coronary blocked patients as well as after treatment is essential in sequence wise to understand the improvement of coronary vascular plagues openings and% of opening. Because the variation in conduction is reflected from blockage, hardening of coronary artery and if also any advance ischemic condition / Myocardial Infarction (MI). In A section before treatment of

ECG graph of a patient point out the high dense noise in atria-ventricular (AV) portion in four graphs in compared to B section after treatment of same patient in figure-4.

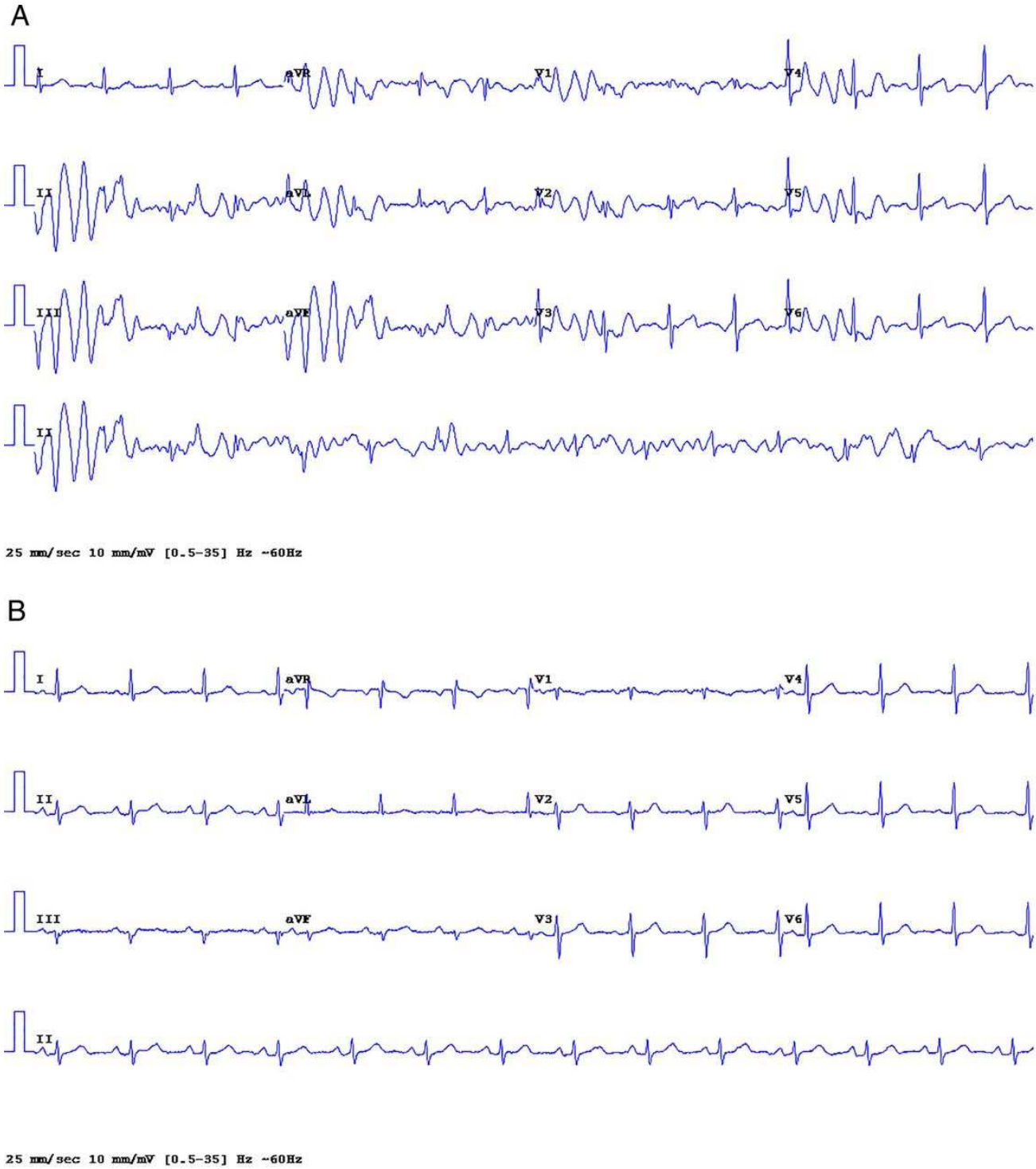

Figure 4. *Improvement of ECG status in a patient in four different state in B section after treatment in compared to A section.*

The ECG graphical trace have been taken after exercise i.e., walking or running on Tread mill test (TMT). Because, TMT is essential for finding the increase cardiac output states and in case if any coronary blockage persist then the variation in QRST peak will mark in graphical way.

Tread mill Test Healthy,

Table 1. *Representation of clinical status of patients on TMT as per Bruce, Modified Bruce & Naughton's methods.*

Functional Class	Clinical Status	O_2 Cost ml/Kg/min	Treadmill Protocols BRUCE MODIFIED 3 min Stages	MPH	% GR	BRUCE 3 min Stages	MPH	% GR	NAUGHTON 2 min stages	MPH	% GR
			6.0		22	6.0		22			
Normal and I			5.5		20	5.5		20			
			5.0		18	5.0		10			
		56.0									
		52.0									
		49.0									
	Healthy,	45.5	4.2		16	4.2		16			
	Dependent	42.0									
	on Age	38.5									
	Activity	35.0	3.4		14	3.4		14			
		31.5							2		17.5
		28.0							2		14.0
	Sedentary Healthy	24.5	2.5		12	2.5		12			
		21.0							2		10.5
II		17.5	1.7		10	1.3		10	2		7.0
III	Limited	14.0							2		3.5
	Symtomatic								2		0
		10.5	1.7		05						
		7.0							1		0
		7.5	1.7		0						
IV		3.5									

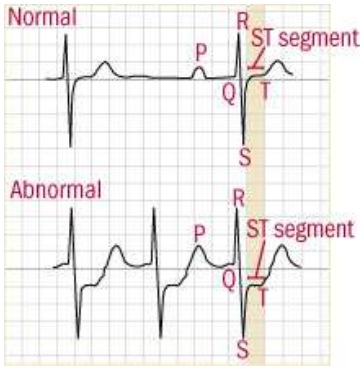

Figure 5. *Difference of ST segment from baseline on cardiac blogged & after treatment.*

The Bruce Treadmill Test is an indirect test that estimates volume of Oxygen (VO_2) max using a formula rather than using direct measurements that require the collection and measurement of the volume and oxygen concentration of inhaled and exhaled air. This determines how much oxygen the athlete (on exercise) is using. The Bruce Protocol is a maximal exercise test where the athlete works to complete exhaustion as the treadmill speed and incline is increased every three minutes (Table-1). The length of time on the treadmill is the test score and can be used to estimate the VO_2 max value. During the test, heart rate, blood pressure and ratings of perceived exertion are often also collected.

Bruce multistage maximal treadmill protocol has 3min periods to achieve steady state before workload is increased. In older individuals or those whose exercise capacity is limited, it can be *modified* by two 3 min warm up stages at 1.7mph and 0 percent grade and 1.7mph and 5%grade. This protocol it is most often used in older individuals or those whose exercise capacity is limited by cardiac disease.

The Naughton and Weber protocols use 1-2min stages with 1-MET (Metabolic equivalent test: In current use it refers to a unit of Oxygen uptake in a sitting, resting patient; 1-MET is equivalent to 3.5 ml O_2/kg/min determines the number of METs associated with activity) increments between stages, this protocol is suitable for patients with limited exercise tolerance such as patients has compensate Congestive Heart failure.

Asymptomatic cardiac ischemia pilot trial and modified ACIP protocols use 2min stages with 1.5 METs increments between stages after two 1min warm up stages with 1-MET increments.

3.2. Doppler Test

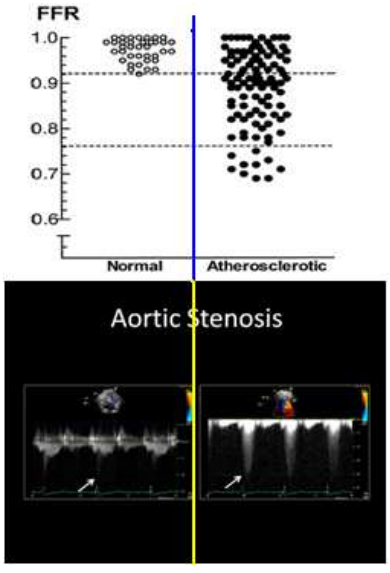

Figure 6. *The difference between the normal and blockage aortic stenosis zone on relating FFR and Doppler scans.*

To detect the blockage of coronary arteries high-frequency sound waves to measure the amount of blood flow through your arteries and veins, usually those that supply blood to arms and legs. And Fractional flow reserve (FFR) is a technique used in coronary catheterization to measure pressure differences across a coronary artery stenosis (narrowing, usually due to atherosclerosis) to determine the likelihood that the stenosis impedes oxygen delivery to the heart muscle (myocardial ischemia). So, through sound analysis as well as pressure response, the Normal morphology of coronary artery could be differentiates from Atherosclerotic vessels in Figure-6 with FFR density graphical representation and Doppler scanned peaks. Here, in this figure-6 left portion is the normal condition artery in compare to right portion of Atherosclerotic vessels due to high interruption noise of sound created by the collision of RBC in narrow stenosis zone.

Doppler test is readily done here to identify the percentage of blockage on analyzing the AUC of electro amplified peaks against the obstacle of flowing RBCs which transmits sound wave frequency. Denser the obstructions wider the peaks wavelength and vice-versa, thus more pressure and more friction is exist. The A & C reveals stenosis of coronary arteries occurs before treatment which was reduce after the cardiac patch treatment into B & D with narrow peaks, after going through Doppler test analysis scans which is shown in Figure-7 Doppler scan images.

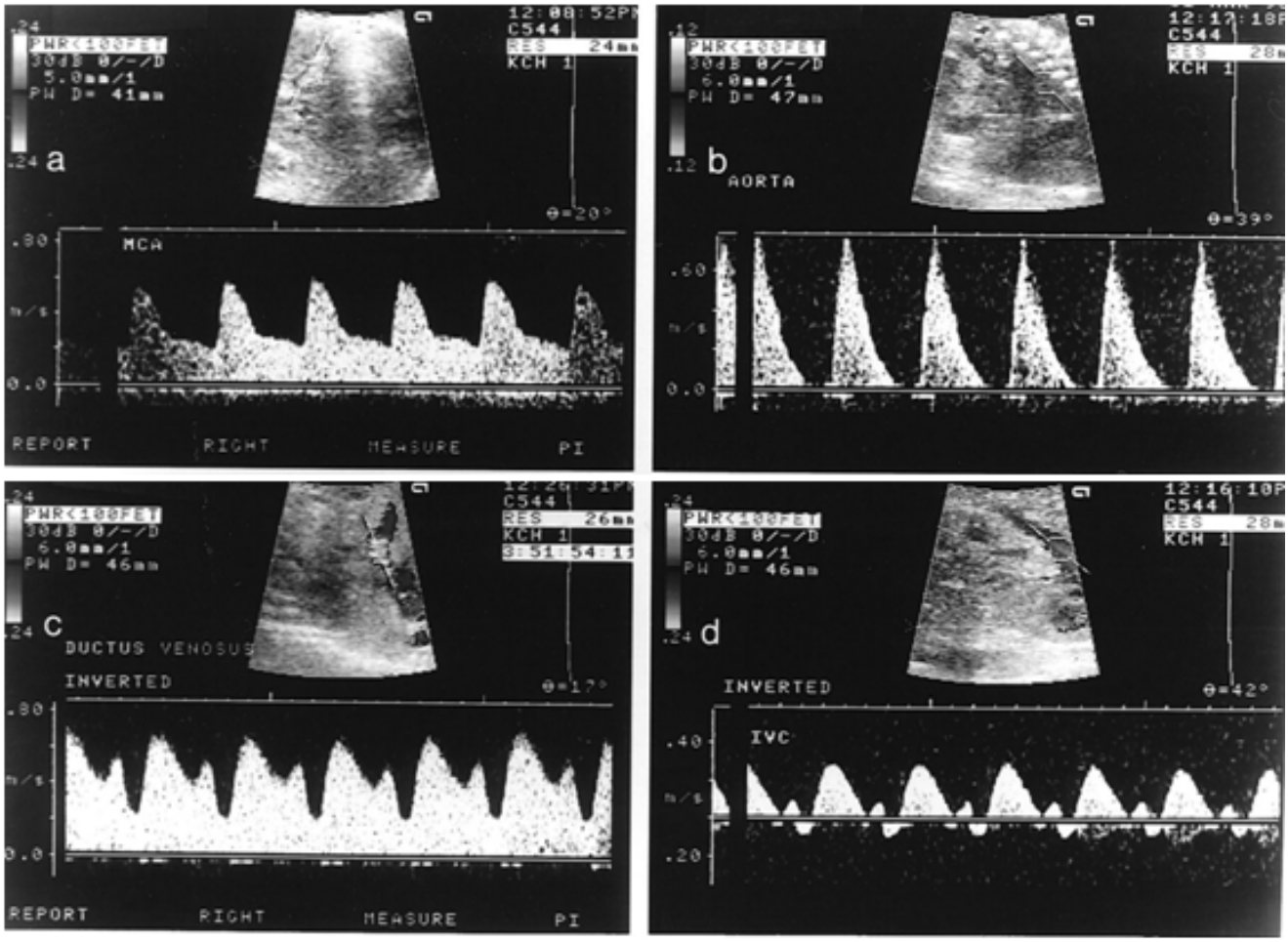

Figure 7. *The comparative Doppler scan of coronary artery before (A&C) and after treatment (B&D) with cardiac patches.*

3.3. Angiogram Analysis

An angiogram is an X-ray test that uses a special dye and camera (fluoroscopy) to take pictures of the blood flow in an artery. Through angiogram it is easier to detect the exact position and extent of blockage in arteries and veins or coronary arteries. Till date 50%-90% blockage was rectified through Coronary Artery Bypass Grafting (CABG) after getting detected on Angiogram report. There is no medicine till to open 50%- 90% blockages of coronary arteries. But the design of electromagnetic cardiac patches recruits the function of direct intrusion of drug formulation through vibratory mechanics. This implies the influx of high concentration of garlic and digitalis to targeted coronary arteries bypassing the vascular systemic circulation network. So, in the Figure-8 shows the angiogram images acquires 70-80% of the blockage before treatment was opened by cardiac patches to 100% without any CABG.

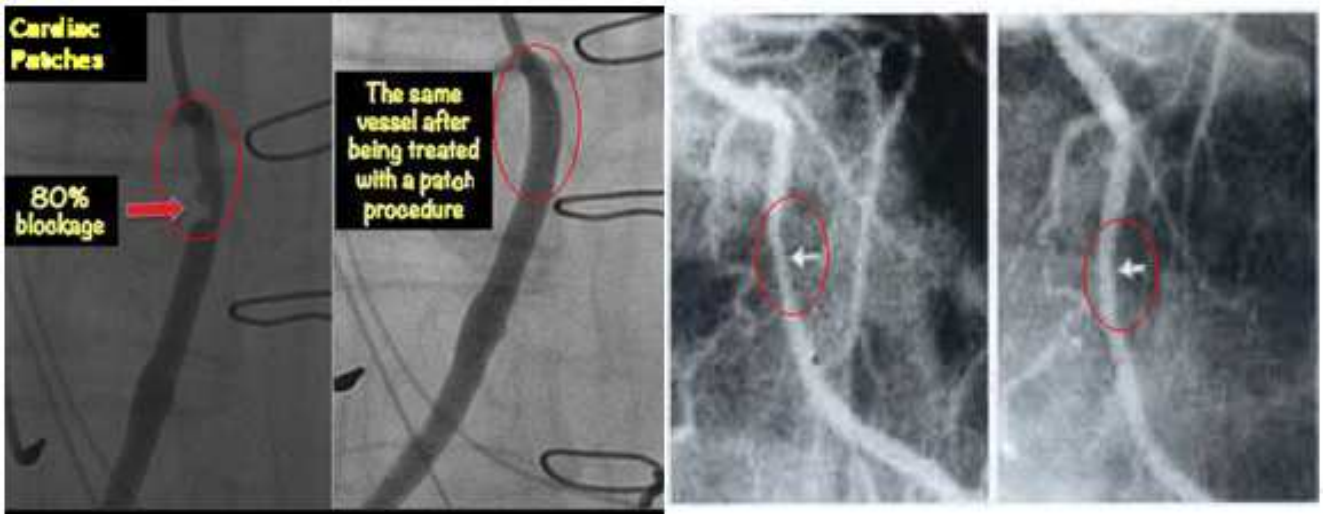

Figure 8. *Angiogram of 70-80% blockage on right side of image has rectified to left side after treatment in both images.*

4. Conclusion

Till date there is neither anti-coagulant, thrombolytic nor antiplatelet drugs which can open the coronary plagues from arteries nor any anti-lipidaemics (eg, Statins) in combination to act a synergistic effects to recue from atherosclerosis. Cardiac patches were a new formulation dosage design with herbal combination of Allicin and TA aqE, satisfies the above treatment. Before the development of Cardiac patches medical science has to rely only on Coronary artery bypass graft [CABG] operation to ratify the coronary 50-80% blockage by removing the plagues. Which can simplified without going through surgery and very less expansive could be afford by any economic compromised patients. This design was successfully operated in patient volunteers after analyzing the support from ECG, TMT, Doppler test & Angiogram analysis.

References

[1] Anna L. H., Madeleine N., Benjamin B., Richard S. Outcomes of coronary artery bypass graft Surgery. Vascular Health and Risk Management 2006: 2(4) 477–484.

[2] Henderson RA, Jarvis C, Clayton T, Pocock SJ, Fox KAA. 10-year mortality outcome of a routine invasive strategy versus a selective invasive strategy in non-ST-segment elevation acute coronary syndrome: the British Heart Foundation RITA-3 randomized trial. J Am College of Cardiology, 2015; 66: 5; 11–20.

[3] Fox KAA, Clayton TC, Damman P, et al. Long-term outcome of a routine versus selective invasive strategy in patients with non-ST-segment elevation acute coronary syndrome: a meta-analysis of individual patient data. J Am College of Cardiology, 2010; 55: 24; 35–45.

[4] Eagle KA, Lim MJ, Dabbous OH, et al. A validated prediction model for all forms of acute coronary syndrome. JAMA 2004; 291: 2727–33.

[5] Gray HH, Henderson RA, de Belder MA, Underwood SR, Camm AJ. Early management of unstable angina and non-ST-segment elevation myocardial infarction: summary of NICE guidance. Heart 2010; 96: 1662–8.

[6] Kureshi F, Jones PG, Buchanan DM, Abdallah MS, Spertus JA. Variation in patients' perceptions of elective percutaneous coronary intervention in stable coronary artery disease: cross sectional study. BMJ 2014; 349: 5309.

[7] M. Diodato and E. G. Chedrawy. Coronary Artery Bypass Graft Surgery: The Past, Present, and Future of Myocardial Revascularization. Surgery Research and Practice, Volume 2014, Article ID 726158, 6 pages (http://dx.doi.org/10.1155/2014/726158).

[8] Gaikwad A. K. Transdermal drug delivery system: Formulation aspects and evaluation. Comprehensive Journal of Pharmaceutical Sciences. 2013; 1 (1); 1 - 10.

[9] Nirav S Sheth, Rajan B Mistry. Formulation and evaluation of transdermal patches and to study permeation enhancement effect of eugenol. Journal of Applied Pharmaceutical Science, 2011: 1 (3); 96-101.

[10] D. Patel, Sunita A. Chaudhary, B. Parmar, N. Bhura. Transdermal Drug Delivery System: A Review. The Pharma Innovation. 2012, 1 (4), 66-76.

[11] Latheeshjlal. L, P. Phanitejaswini, Y. Soujanya, U. Swapna, V. Sarika, G. Moulika. Transdermal Drug Delivery Systems: An Overview. Int. J. Pharm Tech Res. 2011, 3 (4), 2140-48.

[12] S. Dhiman, T. G Singh and A. K. Rehni. Transdermal patches: A recent approach to new drug delivery system. Int J Pharm Pharm Sci, 3 (5), 26-34.

[13] K. Hansen, et al. Microneedles as a transformative technology in drug delivery. Copyright © 2013 Frederick Furness Publishing Ltd, page 8-10.

[14] Gill H, Prausnitz MR. Coated micro needles for Transdermal Delivery. J Control Release, 2007, 11 (7), 227–237.

[15] Lee JW, Park J-H, Prausnitz MR. Dissolving microneedles for transdermal drug delivery. Biomaterials, 2008, 29, 2113–2124.

[16] Teo A, Shearwood C, Ng K, Lu J, Moochhala S. Transdermal micro needles for drug delivery application. Materials Sci. Eng, 2006, 13 (2), 151–154.

[17] Stoeber B, Liepmann D. Arrays of hollow out-of-plane microneedles for drug delivery. J Microelectromechanical Systems, 2005, 14, 472–479.

[18] Yung K, Xu Y, Liu H, Tam K, Ko S, Kwan F, Lee Y, Sharp-tipped plastic hollow microneedle array by microinjection moulding. J Micromechanical Micro eng, 2012, 22, 1–10.

[19] Lhernould MS, Delchambre A. Innovative design of hollow polymeric microneedles for transdermal drug delivery. Microsystem Technol, 2011, 17, 1675–1682.

[20] Burton S, Moeckly C, Brandwein D, Gilbert T et al. Rapid intradermal delivery of liquid formulations using a hollow microstructured array. Pharm Res, 2011, 28, 31–40.

[21] Lhernould MS, Lambert P. Compact polymer multinozzle electrospray device with integrated microfluidic feeding system. J Electrost. 2011, 69, 313–319.

[22] Verbaan F, Van den Berg D, Dijksman J. Improved piercing of microneedle arrays in dermatomed human skin by an impact insertion method. J Control Release, 2008, 128, 80–88.

[23] Pacini S, Punzi T, Gulisano M. Transdermal delivery of Hyaluronicaci. J of Dermatology Sc, 2006, 44, 169-171.

[24] Pacini S, Punzi T, Gulisano M. Transdermal delivery of Clostridium Botulinum Toxin Type A by pulsed current Iontophoresis. Poster Presented at 65th Annual Meeting of the American Academy of Dermatology, 2007, Washington DC, US.

[25] Pacini S., Punzi T, Gulisano M et al. Transdermal deliveryof heparin using pulsed current inotophoresis. Pharm Research, 2006, 23 (1), 114-120.

[26] Pacini S, Peruzzi B, Gulisano M. Qualitative and quantitative analysis of transdermic delivery of different biological molecules by iontophoresis. Italian Journal of Analt Embryol, 2003, 18 (2), 127–129.

[27] Pacini S., Peruzzi B, Gulisano M et al. Transdermal delivery of heparin by means of alternate current skin electroporation". Ital J Anat Embryol, 2004, 109 (1), 223.

[28] De Bartolo HM, "Comparison of Mattioli Iontophoresis, Mesosystems, the U225, and Manual Injections". Proceedings of the Illinois Society of Ophtalmology & Otolaryngology, 2005, Vol 9 (1).

[29] De Bartolo HM, "Scar Revision &Minimally Invasive Cosmetic Surgery using Mattioli Engineering Technology", ibid.

[30] Bacci PA, "The role of Dermo electroporation". Cellulite: Pathphysiology & Treatment, 2006, Chapter 18, pp 291-299. (Published by Taylor & Francis, ISBN-10: 0-8247-2985-4/ISBN-13: 978-0-8247-2985).

[31] Gonen A, Harats D, Rabinkov A, Miron T, et al. The antiatherogenic effect of allicin: possible mode of action. Pathobiology. 2005; 72 (6): 325-34.

[32] Laham RJ, Simons M, Hung D et al. Subxyphoid access of the normal pericardium: a novel drug delivery technique. Catheter Cardiovasc Interv. 1999 May; 47 (1): 109-11.

[33] Theofilos M. Kolettis, Nikolaos Kazakos, Christos S. Katsouras et al. Intrapericardial drug delivery: pharmacologic properties and long-term safety in swine. Int J Cardiol. 2005 Mar 30; 99 (3): 415-21.