EUROPEAN JOURNAL OF BIOMEDICAL AND PHARMACEUTICAL SCIENCES
http://www.ejbps.com

ISSN 2349-8870
Volume: 3
Issue: 6
268-275
Year: 2016

REVIEW ON SIDDHA MEDICINAL PLANTS AND FORMULATIONS WITH THROMBOLYTIC ACTIVITY

Vidhya Somasundaram*[1], Ramani Mani[2], Tamil Muhil Mathavan Kaarthikeyan[3], Saravana Singh Karan, Chand Mohan Singh[4]

[1,2]Research Scholar, Post Graduate Department of Gunapadam (Pharmacology), Government Siddha Medical College, Chennai. Tamilnadu, India.
[3]Research Scholar, Post Graduate Department of Kuzhanthai Maruthuvam (Pediatrics), Government Siddha Medical College, Chennai. Tamilnadu, India.
[4] Siddha Medical Consultant, no. 10, Kattabomman Main Road, Kodungayur, Chennai-51. Tamilnadu, India.

*** Corresponding Author: Vidhya Somasundaram**
Research Scholar, Post Graduate Department of Gunapadam (Pharmacology), Government Siddha Medical College, Chennai. Tamilnadu, India.

Article Received on 02/04/2016 **Article Revised on 22/04/2016** **Article Accepted on 12/05/2016**

ABSTRACT
Thrombotic diseases myocardial infarction or cerebral infarction is serious consequences of the thrombus formed in blood vessels. Thrombolytics are the drugs to lyse thrombi to recanalize occluded blood vessels. Commonly used thrombolytics are Streptokinase, Urokinase, tissue Plasminogen Activator to dissolve the clots. Currently available thrombolytic agents still have significant shortcomings, including the need for large dose to be maximally effective, limited fibrin specificity & bleeding tendency. These shortcomings present in thrombolytic agents have started to seek the attractive alternative medicines. Siddha have huge source of medicine for various diseases. They mention the different properties of Herbal, Mineral and Herbo – mineral drugs which can be used in different disease by making many combination and formulation. This present review had as its objective the compiling of data based on works carried out in some Siddha Medicinal plants that are consumed frequently by humans & that have demonstrated thrombolytic activity.

KEYWORDS: Thrombotic diseases, Thrombolytic activity, Thrombolytics, Siddha Medicinal plants.

INTRODUCTION
A thrombus formed in the blood vessel due to the failure of hemostasis result in vascular blockage and while recovering leads to serious consequences in atherothrombotic diseases such as Myocardial infarction or Cerebral infarction, at times leading to death.[1] Thrombosis underlies some acute coronary disorders such as pulmonary emboli, Deep Vein Thrombosis, Strokes and Heart attacks and these are the major causes of morbidity and mortality in developed countries.[2] Of the various circulatory disorders, thrombosis represents the major cause of death globally, affecting millions of people with annual incidence rates varying from 1 per 10,000 young adults to 1 per 100 elderly persons.[3]

Thrombolytics are the drugs to lyse thrombi to recanalize occluded blood vessels (mainly coronary artery). They are curative rather than prophylactic; work by activating the natural fibrinolytic system. Commonly used thrombolytics are Streptokinase (SK), Urokinase (UK), tissue Plasminogen Activator (tPA) to dissolve the clots.[4] Therefore thrombolytics are considered as a key tool in the treatment of Cardio vascular thrombotic diseases.

In India, though SK and UK are widely used to lower cost, as compared to other thrombolytic drugs (tPA), their use is associated with hyper risk of haemorrhage [5] severe anaphylactic reaction & lacks specificity. Moreover, as a result of immunogenicity multiple treatments with SK in a given patient restricted.[6] Because of the shortcomings of the available thrombolytic drugs, attempts are underway to develop improved recombinant variants of these drugs.[7-11] Currently available thrombolytic agents still have significant shortcomings, including the need for large dose to be maximally effective, limited fibrin specificity & bleeding tendency. These shortcomings present in thrombolytic agents have started to seek the attractive alternative medicines.

Throughout the history, plants are of the important sources of medicine & a plenty of drugs in use are derived from plants and or their derivatives, & a new plant – derived medicines are continually being discovered. The therapeutic uses of plants are safe, economical & effective as their ease of availability.[12] Medicinal plants are widely used in the traditional system for the treatment of several diseases that contain

chemical compounds which act as precursor for the synthesis of useful drugs.[13] Siddha is an ancient and traditional system of science, which gives basic philosophy of diagnosis, prevention & management of diseases. Siddha have huge source of medicine for various diseases. They mention the different properties of Herbal, Mineral and Herbo – mineral drugs which can be used in different disease by making many combination and formulation.

This present review had as its objective the compiling of data based on works carried out in some Siddha Medicinal plants that are consumed frequently by humans & that have demonstrated thrombolytic activity. With these goals in mind, the authors of this article have attempted to give information to researchers who are exploring compounds with this potential and to encourage the development of new investigations in this area of study.

THROMBOLYTIC MEDICINAL PLANTS

Aegle marmelos
Family: Rutaceae
Tamil Name: *Vilvam*
Common Name: Bael tree
Part Used: Leaves

Thrombolytic activity
Aegle marmelos leaf extract using a simple and quick in vitro clot lysis assay was performed which exhibited maximum 84% clot lysis at 800 µg/ml concentration in 90 mins and incubation at 37ºC.Various concentrations of leaf extract i.e. 200 µg/ml,400 µg/ml and 800 µg/ml where tested at time intervals of 90 mins and incubation37ºC for observing maximum clot lysis.The results findings indicated that concentrations of leaf extract enhanced the percentage of clot lysis in dose dependent manner However; SK and water were used as a positive and negative control showed clot lysis maximum 89% and 2% in 90 mins of incubation respectively.[14]

Andrographis paniculata
Family: Acanthaceae
Tamil Name: *Nilavembu*
Common Name: Green chiretta kalmegh
Part Used: Aerial part

Thrombolytic activity
To evaluate the thrombolytic activity of (Dichloromethane: Methanol), chloroform and methanol extracts of aerial parts of Andrographis paniculata by in vitro method. Among the 3 extracts multiple solvent extract have shown a significant (73.01%) clot lysis and when compared with standard drug (SK) it showed similar activity. Hence, it may be concluded that the multiple solvent extract of aerial parts of Andrographis paniculata having thrombolytic activity.[15]

Bacopa monnieri
Family: Scrophulariaceae
Tamil Name: *Neer brahmmi*
Common Name: Thyme leafed gratiola
Part Used: Leaves

Thrombolytic activity
To evaluate the thrombolytic activity of ethanolic, methanolic, acetone and aqueous extracts of root, stem and leaf of Bacopa monnieri by in vitro method. Extraction was carried out using Soxhlet apparatus. The leaf ethanolic extract showed highest thrombolysis followed by aqueous, methanol and acetone extract. Concentration of phytochemicals and incubation time were directly propotional to the clot lysis.[16]

Chloroform extract of Bacopa monnieri displayed significant thrombolytic properties in different blood samples. The mean percent thrombolytic activity of chloroform plant extract of Bacopa monnieri was found to be 48.39%, When compared with positive (SK-85.77%) and negative control (water-4.70%).[17]

Brassica oleracea flower
Family: Brassicaceae
Common Name: Cauliflower
Part Used: Flower

Thrombolytic activity
The study was evaluated the thrombolytic activity of methanol extract of the flower of Brassica oleracea by in-vitro method. Extract of the plant showed (42.75± 3.72%) thrombolytic compared with standard Streptokinase's (67.32±5.25%) clot lytic activity in case of thrombolysis assay.[18]

Camellia sinensis
Family: Theaceae
Common Name: Green tea
Part Used: Leaves

Thrombolytic activity
Thrombolytic activity of crude water, ethanol and acetone extracts of Camellia sinensis (green tea) leaves in vitro. Rapid methodology was validated to discover thrombolytic effect of water, ethanol and acetone extracts of Camellia sinensis leaves where SK and water were used as a positive and negative controls, respectively. The percentage of clot lysis was statistically significant ($p<0.0001$) when compared with negative control.

Using an in vitro thrombolytic model, water, ethanol and acetone extracts of Camellia sinensis (green tea) leaves revealed moderate thrombolytic activity(45.60±2.313%, 37.68± 2.211% and 30.51% ±2.551%, respectively) whereas standard SK demonstrated 87.15± 3.212% thrombolytic effect and negative control water showed 5.60± 2.131% clot lysis of clot.[19]

Carica papaya
Family: Caricaceae
Tamil Name: Pappaali
Common Name: Papaya
Part Used: Root, leaf and seed

Thrombolytic activity
To investigate the thrombolytic activity of aqueous extract of Carica papaya (root, seed and leaf) parts. SK was used as a positive control. The human blood was taken as test sample. The mean % of clot lysis for SK was 36.44%.Similarly, the root, seed and leaf extracts of Carica papaya showed the mean% of clot lysis as 24.70%, 24.29% and 23.67% respectively. When all this three extracts were compared with SK, they were significant at $p<0.05\%$.[20]

Commelina benghalensis
Family: Commelinaceae
Tamil Name: *Kaanaam vaazhai*
Common Name: Blue Spider wort
Part Used: Leaves

Thrombolytic activity
In this study, methanolic extracts of the leaves of Commelina benghalensis was subjected to assess the thrombolytic activity by in vitro model. The results were compared with standard drug SK. Addition of 100 µl SK to the clots along with 90 mins at the incubation of 37°C, showed (75±0.09%) clot lysis. clots when treated with 100µl of sterile distilled water (control) revealed negligible (4.19±0.12%) clot lysis effect. Methanol extract of leaves of Commelina benghalensis showed thrombolytic activity was 40.94±0.78%.[21]

Delonix elata
Family: Fabaceae
Tamil Name: *Vaadha narayanan*
Common Name: White Gul Mohur, yellow Gul Mohur
Part Used: Leaves

Thrombolytic activity
The study was to evaluate the thrombolytic activity by in vitro method of aqueous and ethanolic extracts of the leaves of Delonix elata. The thrombolytic activity was investigated by the addition of the test material to the pre-clotted blood that was incubated for 90 mins at 37°C & was expressed as percentage of clot lysis. The aqueous and ethanolic extracts of leaves of Delonix elata displayed a dose dependent thrombolytic effect ranging from 6.90% to 17.12% and 5.08% to 12.33%, respectively. It was found that ethanolic extracts demonstrated higher thrombolytic effect than aqueous extracts. These results are compared with the positive control SK and negative control which displayed a moderate clot lysis of 19.80% and 1.50%, respectively.[22]

Erythrina variegata
Family: Fabaceae
Tamil Name: *Kaliyana murukku*
Common Name: Indian Coral tree
Part Used: Bark

Thrombolytic activity
In this experiment, various extracts of the bark of Erythrina variegata were subjected to evaluate the thrombolytic activity by using human erythrocyte. The results were compared with standard drug SK. Addition of 100 µl SK to the clots along with 90 mins at the incubation of 37°C, displayed 78.42% clot lysis effect. Clots when treated with 100µl of sterile distilled water (control) revealed 3.21% clot lysis. Methanol extract showed highest thrombolytic activity 72.14±3.77%, whereas ethanol and chloroform extracts of the bark of Erythrina variegata revealed moderate thrombotic activities (60.08±2.07% and 55.82±2.48% respectively).[23]

Lablab parpureus
Family: Fabaceae
Tamil Name: *Avarai*
Common Name: Bean
Part Used: Leaves

Thrombolytic activity
The leaves extracts of Lablab parpureus were subjected to the thrombolytic activity was evaluated by using human erythrocyte and the results were compared with standard SK. Addition of 100 µl SK, a positive control, to the clots and subsequent incubation for 90 mins at 37°C,revealed 93.29% lysis of clot. At the same time, distilled water was used as a negative control which exhibited negligible clot lysis (4.74%). In this study, the carbon tetrachloride soluble fraction (CCSF) demonstrated highest thrombolytic activity (51.60%), Ethanolic fraction (EF) showed 41.81% clot lysis effect and n-hexane soluble fraction (HSF) revealed 22.47% lysis of clot.[24]

Mesuea ferrea
Family: Cluciaceae
Tamil Name: *Naagapoo*
Common Name: Cobra Saffron
Part Used: Leaves

Thrombolytic activity
Methanolic extract of leaves of Mesuea ferrea was used to evaluate the thrombolytic effect of the various fractions was investigated in clot lysis experiment. The extract exerted 36.32% clot lysis of the blood in the thrombolytic activity test while 85.45% and 7.5% lysis were obtained for positive control (SK) and negative control respectively. So, the methanolic extract of leaves of Mesuea ferrea possessed considerable thrombolytic activity.[25]

Momordica charantia
Family: Cucurbitaceae
Tamil Name: *Paagal*
Common Name: Bitter gourd
Part Used: Fruits

Thrombolytic activity
Thrombolytic investigation involved five young volunteers to get different type of blood samples. Five concentrations of crude ethanolic extract of Momordica charantia fruit were used for the study, with SK as standard, sterilized distilled water as a negative control to validate the method. Thrombolytic activity of the fruit was found significant ($p < 0.01$) except for the concentration 4mg/ml, when compared with negative control (water) at different doses. The fruit showed mild colt lysis, i.e. 2.16± 0.723%, 5.06± 1.058%, 8.60± 0.626%, 11.64± 0.747% and 15.18± 1.691% at 2, 4, 6, 8 and 10mg/ml concentrations respectively, while SK showed 47.22± 2.738% clot lysis. From the above results suggest that the crude ethanolic extract of Momordica charantia fruit possess mild thrombolytic activity in vitro.[26]

Nigella sativa
Family: Ranunculaceae
Tamil Name: *Karunchirakam*
Common Name: Black Cumin
Part Used: Seeds

Thrombolytic activity
An in-vitro method was adopted to check the thrombolytic activity of seeds of Nigella sativa against SK as a positive control. It was found that after addition of SK, clot formation is delayed up to more than 90 mins. Different concentrations of Nigella sativa extract delayed the clot formation. The maximum delay in the clot formation of 27 min was recorded at 1.00 mg/dl. For thrombolytic activity, at this concentration the clot dissolution time was 79 min with aqueous extracts.[27]

Punica granatum
Family: Punicaceae
Tamil Name: *Maadhulai*
Common Name: Pomegranate
Part Used: Fruit and exocarp

Thrombolytic activity
Ethanolic and aqueous extract of fruit and peel of the Punica granatum was used for in vitro clot lysis activity. Streptokinase (SK) was used as standard. In a series of pre-weighed eppendorf tubes, equal volume of venous blood was collected & serum was removed and the tubes were weighed. The tubes containing clot were incubated with fruit, peel extract (100 µg/ml) and SK individually at 37^{o}C for 60 minutes. After incubation, fluid was removed and tubes were again weighed to observe the difference in weight after clot disruption. The percentage of clot lysis was determined. Of the extracts, ethanolic extract showed maximum activity compared with aqueous extract. Maximum Thrombolytic activity 59% was observed with ethanolic extract of peel of the fruit (ascorbic acid).[28]

Swertia chirata
Family: Gentianaceae
Tamil Name: *Siratkuchii*
Common Name: Bitter stick
Part Used: Stick

Thrombolytic activity
Ethanol extract of Swertia chirata was evaluated for its thrombolytic activity by in-vitro method. Clot lysis assay method was used for in vitro thrombolytic study. The crude ethanol extract was found to have significant thrombolytic test revealed a maximum effect of 40.38% when compared with the standard drug SK (69.35%).[29]

Tamarindus indica
Family: Caesalpiniaceae
Tamil Name: *Puli*
Common Name: Tamarind tree
Part Used: Fruit pulp

Thrombolytic activity
In –vitro evaluation of Thrombolytic activity of Tamarindus indica pulp of fruits in three extracts, Ethanol, Acetone and DM water extract. SK and Water were used as a positive and negative control respectively. From the experiment DM water showed 2.1% of clot lysis. Thrombolytic property of SK revealed 86.3%. Ethanol extract of pulp of Tamarindus indica and DM water extract of pulp showed 57% and 55.3% clotlysis respectively. Acetone extract revealed 52.9% of clotlysis property.[30]

Terminalia bellerica
Family: Combretaceae
Tamil Name: *Tanrikkai*
Common Name: Beleric Myrobalans
Part Used: Fruits

Thrombolytic activity
An in vitro method was used to demonstrate the clot lysis effect of the fruits of Terminalia bellerica along with SK as a positive control. From this study, at the concentration of 1.00 mg/ dl the clot dissolution time is minimum i.e. 58nand 66 mins for aqueous and alcoholic extracts respectively. From this above study, it was found that the fruits of Terminalia bellerica possess thrombolytic activity in vitro.[31]

Withania somnifera
Family: Solanaceae
Tamil Name: Amukkura kizhangu
Common Name: Winter cherry (Ashwagandha)
Part Used: Root Thrombolytic activity:

The root extracts of Withania somnifera were subjected to the thrombolytic activity on human blood sample. The

thrombolytic activity was evaluated by using human erythrocyte and the results were compared with standard drug SK.

Addition of 100µl SK standard to the clots along with 90 mins of incubation at 37°C, showed 66.77% of clot lysis. Clots when treated with 100µl sterile water (control) showed negligible clot lysis (2.64%). The methanol extract revealed the highest thrombolytic activity (68.14%). Whereas the extracts of ethanol and chloroform of the root of Withania somnifera showed moderate (21.15% and 17.64%) thrombolytic activities.[32]

S. No	Name of the plant	Tamil name	Common name	Part Used	Remarks
1	Acacia nilotica	*Karuvel*	Black Babool	Root	Addition of 500 µl of SK of 30,000 IU and 15,000 IU concentrations to tubes showed highly significant (P< 0.001) clot lysis of 47.21% and 24.73% respectively comparing with 5.35% clot lysis of normal saline considered as a negative control. At 5mg/ml concentration of root extract of Acacia nilotica showed 15.1% of thrombolysis activity.[33]
2	Anacardium occidentale	*Muntiri*	Cashew nut		Thrombolytic activity of Aqueous extract of Anacardium occidentale revealed 33.79 ± 2.926%.[34]
3	Azadiracta indica	*Vembu*	Neem		Clot lysis effect of Aqueous extract of Azadiracta indica displayed 27.47± 6.943% by using in-vitro method.[33]
4	Curcuma longa	*Manjal*	Turmeric		An in-vitro thrombolytic model was used to check the clot lysis effect of aqueous extract of Curcuma longa along with SK & Water used as a positive and negative control. The percentage (%) of clot lysis was statistically (p<0.0001) showed 32.94±3.663%[34]
5	Glycyrhiza glabra	*Adhimadhuram*	Liquorice		An in-vitro thrombolytic model was used to check the clot lysis effect of aqueous extract of Glycyrhiza glabra showed 17.8 ± 3.4 % of clot lysis along with reference to SK (86.2%)[35]
6	Hemedesmus indicus	*Nannaari*	Indian Sarsaparilla		Aqueous extract of Hemedesmus indicus revealed 20.3 ± 5.7 % of clotlysis along with SK and water were used as a positive and negative control respectively [35]
7	Justicia adhatoda	*Aadathoda*	Malabar-nut	Root	Clot lysis effect of Root extract of Justicia adhatoda showed 19.63% which was comparing with SK (positive control) and Normal saline (negative control)[33]
8	Ocimum sanctum	*Thulasi*	Holy basil		Addition of 100 µl SK, a positive control to the clots along with 90 minutes of incubation at 37°C, revealed 86.2% clot lysis. Clots when treated with 100 µl sterile distilled water (negative control) showed 4.7% clot lysis. After treatment of clots with 100 µl of Ocimum sanctum showed moderate thrombolysis i.e.30.01±6.168%[34]
9	Rubia cordifolia	*Manjiti*	Indian Madder		In vitro method of thrombolytic activity of Rubia cordifolia displayed 14.5 ± 3% of clot lysis[35]
10	Tinospora cordifolia	*Seendhil*	Heart leaved Mooseed		Aqueous extract of Tinospora cordifolia showed 19.3 ± 3.4% of thrombolytic activity by using in vitro model[35]

SIDDHA FORMULATIONS

Ayanaga parpam[36]
Eggu chendhooram[37]
Kaandha parpam[38]
Sembu Chenndooram[39]
Naaga parpam[40]
Sangu parpam[41]
Palagarai chendooram[42]
Navaneetha parpam[43]
Inji nei[44]
Vellaipoondu ilagam[45]
Mudakkothan Ennai [46]
Mudakothhan nnnai[47]
Veera mezhugu[48]
Thaamira chendooram[49]
Kaalamega narayana chendooram[50]
Sadatchara akkini kumaaran[51]
Kariuppu chendooram[52]
Panchalavana parpam[53]
Arugam ver thylam[54]
Maharaja mirugaangam[55]
Mahavasantha kusumaharam[56]
Appiraga parpam[57]
Soodha parpam[58]
Sirungi parpam[59]
Sirungi chendooram[60]

REFERENCES

1. Collen D. Coronary thrombolysis: streptokinase or recombinant tissue-type plasminogen activator, Annals of Internal Medicine, 1990; 112: 529-538.
2. Watson RDS, Chin BSP, Lip GYH, BMJ, 2002; 325: 1348-1351.
3. Adiba, M., Jahan, N., Hussain, I.M. & Nazamuddin. Evaluation of antithrombotic activity of Doqu (Peucedanum grande CB Clarke) in animal model. World Journal of Pharmacy and Pharmaceutical Sciences, 2013; 5: 3915-3928.
4. Gesler WM. Therapeutic landscapes: medical issues in light of the new cultural geography, Social Science & Medicine, 1992; 34: 735-746.
5. Rouf SA, Moo-Young M, Chisti Y. Tissue-type plasminogen activator: characteristics, applications and production technology. Biotechnoogy Advances, 1996; 14(3): 239-66.
6. Jennings K. Antibodies to streptokinase. British Medical Journal, 1996; 312(7028): 3934.
7. Adams DS, et al, A synthetic DNA encoding a modified human urokinase resistant to inhibition by serum plasminogen activator inhibitor. Journal of Biological Chemistry, 1991; 266(13): 8476-82.
8. Lijnen HR et al, On the mechanism of fibrin-specific plasminogen activation by staphylokinase. Journal of Biological Chemistry, 1991; 266(18): 11826-32.
9. Marder VJ: Recombinant streptokinase: opportunity for an improved agent. Blood coagulation and Fibrinolysis, 1993; 4(6): 1039-40.
10. Nicolini FA et al.: Sustained reflow in dogs with coronary thrombosis with K2P, a novel mustant of tissue-plasminogen activator. Journal of the American College of Cardiology, 1992; 20(1): 228-35.
11. Wu DH, et al.: Coiled oil region of streptokinase gamma-domain is essential for plasminogen activation. Journal of Biological Chemistry, 2001; 276(18): 15025-33.
12. Kumar V., Andola H.C., Lohani H. and Chauhan N. (2011). Pharmacological Review on Ocimum sanctum Linnaeus: A Queen of herbs. J of Pharm Res, 4: 366-368.
13. Sofowora A. Medicinal Plants And Traditional Medicine In Africa. John Wiley and sons Ltd., 1982.
14. Pushplata Chougule, Vishal Jain, Avinash Suryawanshi, Ashish Jain, Screening of Thrombolytic Activity of Aegle marmelos Linn leaves Extract by in vitro, International Journal of Pharmaceutical Sciences Review and Research, 2014; 28(1): 176-178.
15. S. Eugine Leo Prakash, R. Manavalan, An investigation of Andrographis paniculata for thrombolytic activity by in vitro method, Journal of Pharmacy Research, 2011; 4(6): 1934.
16. Sai Sandeep, Mamata panigrahi et al.: Evaluation of in vitro thrombolytic activity of phytochemicals in Bacopa monneri, Journal of Pharmacy Reasearch, 2012; 5(1): 100-101.
17. Joysree Das and Md. Muradur Rahman, Bulletin of Pharmaceutical Research, 2014; 4(3): 133-9.
18. A.T.M. Mostafa Kamal, Kazi Ashfak Ahmed Chowdhury et al.: Phytochemical Screening, Cytotoxic and Thrombolytic Activity of Extract of Brassica oleracea Flower (Caulif lower), Global Journal of Pharmacology, 2015; 9(1): 115-120.
19. Mir Monir Hossain and Shahrin Mahmood, In vitro Studies on Antibacterial, Thrombolytic and Antioxidant Activities of Green tea or Camellia sinensis, American Journal of Phytomedicine and Clinical Therapeutics, 2014; (2)(10): 1200-1211.
20. Kalaiyarasi. L, Mubben sultana. D, In vitro Study of Thrombolytic Activity by Using Aqueous Preparation of Different Parts of Carica Papaya Plant Extract, Journal of Pharmacy and Biological Sciences, 2014; 9,3(II): 34-39.
21. Thanwir Ahmed Chowdhury, Abul Hasanat et al.: Thrombolytic and Cytotoxic activity of methanolic Extract of Commelina benghalensis leaves, Journal of Scientific and Innovative Research, 2015; 4(2): 100-104.
22. Pakkirisamy Rajkumar, et al.: Evaluation of in vitro thrombolytic activity of Delonix elata leaf extracts, Journal of Natural Products and Biomedical Research, 2015; 1(2): 45-47.
23. Mohammad Shahrihar, Nishat Zareen Khair, Mahjabeen Gazi and Rumana Akhter, In vitro thrombolytic activity of Erythrina variegata bark, World Journal of Pharmaceutical Research, 2015; 4(5): 512-515.
24. Dilara Parvin, Mir Mohammad Nasir Uddin et al,: Phytochemical screenings, thrombolytic activity and anti microbial properties of the leaf extracts of

Lablab Parpureus, American Journal of Research Communication, 2013; 1(2): 49-55.
25. Mohammad Imran Hossain, Md Hossan sakib et al.: Study on in-vitro thrombolytic activity of methanolic extract of Mesua ferrea leaves, International of Medical and Health Research, 2015; 1(2): 52-55.
26. Abhijit Das, Syed Masudur Rahman Dewan et al,: Investigation of in-vitro thrombolytic potential of ethanolic extract of Momordica charantia fruits: An anti-diabetic medicinal plant, Pelagia Research Library, 2013; 4(2): 104-108.
27. Vassem A Ansari, H.H. Siddiqui, R.K. Dixit, Antithrombotic and thrombolytic activity of Nigella sativa seeds extracts, An International Journal of Advances in Pharmaceutical Sciences, 2014; 5(1): 1829-1833.
28. Sampath R, Renuka Saravanan et al: Thrombolytic activity of Punica granatum fruit and peel extract, Asian journal of Pharmaceutical and Clinical Research, 2016; 9(1): 268-271.
29. Mohammad Shahadat Hossain, Mohammad Ehsanul Hoque Chowdhury et al., In-Vitro Thrombolytic and Anti-inflammatory Activity of Swertia chirata Ethanolic Extract, journal of Pharmacognosy and Phytochemistry, 2012; 1(4): 99-104.
30. S.M. Moazzem Hossen, Mohammad Enamul Hoque et al., Thrombolytic & Cyto-toxic Property of Ethanol, Acetone & DM Water extract of Tamarindus indica Linn. Fruits pulp: An In-vitro Evaluation.
31. Vassem A Ansari, H.H. Siddiqui, Satya Prakash Singh, Antithrombotic and thrombolytic activity of Terminalia belerica fruit extracts, Reasearch Journal of Pharmaceutical Biological and Chemical Sciences, 2012; 3(2): 471-477.
32. Mohammad Shahriar, Fariha Alam and Mir Muhammad Nasir Uddin, Membrane Stabilizing and Thrombolytic activity of Withania somnifera Root, American Journal of Phytomedicine and Clinical Therapeutics, 2014; (2)(2): 252-256.
33. Fahad Hussain, Md., Ariful Islam, Latifa Bulbul, Md., et al., In vitro thrombolytic potential of root extracts of four medicinal plants available in Bangladesh, Anc Sci Life., 2014; 33(3): 162-164.
34. Irfan Newaz Khan, Md. Razibul Habib et al., Thrombolytic potential of Ocimum sanctum, Curcuma longa, Azadirachta indica and Anacardium occidentale, Journal of Basic and Clinical Pharmacy, 2011; 2(3): 125-127.
35. Sweta Prasad, Rajpal Singh Kashyap et al., Effect of Fagonia Arabica (Dhamasa) on in vitro thrombolysis, BMC Complementary and Alternative Medicine, 2007; 7: 36 doi:10.1186/1472-6882-7-36.
36. Thiyagarajan. R. Text Book of Materia Medica (Gunapadam) – Thathu & Jeevam, Published by Department of Indian Medicine and Homoeopathy, 2008; 106.
37. Thiyagarajan. R. Text Book of Materia Medica (Gunapadam) – Thathu & Jeevam, Published by Department of Indian Medicine and Homoeopathy, 2008; 113.
38. Thiyagarajan. R. Text Book of Materia Medica (Gunapadam) – Thathu & Jeevam, Published by Department of Indian Medicine and Homoeopathy, 2008; 133.
39. Thiyagarajan. R. Text Book of Materia Medica (Gunapadam) – Thathu & Jeevam, Published by Department of Indian Medicine and Homoeopathy, 2008; 158.
40. Thiyagarajan. R. Text Book of Materia Medica (Gunapadam) – Thathu & Jeevam, Published by Department of Indian Medicine and Homoeopathy, 2008; 167.
41. Thiyagarajan. R. Text Book of Materia Medica (Gunapadam) – Thathu & Jeevam, Published by Department of Indian Medicine and Homoeopathy, 2008; 646.
42. Thiyagarajan. R. Text Book of Materia Medica (Gunapadam) – Thathu & Jeevam, Published by Department of Indian Medicine and Homoeopathy, 2008; 682.
43. Thiyagarajan. R. Text Book of Materia Medica (Gunapadam) – Thathu & Jeevam, Published by Department of Indian Medicine and Homoeopathy, 2008; 714.
44. V. Kandhasami Mudhaliyar, Padhinen Siddhar Aruliya Aavialikum Amudhamurai Surukkam, -Part-2, Published by Department of Indian Medicine and Homoeopathy, 2011; 217.
45. V. Kandhasami Mudhaliyar, Padhinen Siddhar Aruliya Aavialikum Amudhamurai Surukkam, -Part-2, Published by Department of Indian Medicine and Homoeopathy, 2011; 228.
46. V. Kandhasami Mudhaliyar, Padhinen Siddhar Aruliya Aavialikum Amudhamurai Surukkam, -Part-2, Published by Department of Indian Medicine and Homoeopathy, 2011; 232.
47. V. Kandhasami Mudhaliyar, Padhinen Siddhar Aruliya Aavialikum Amudhamurai Surukkam, -Part-2, Published by Department of Indian Medicine and Homoeopathy, 2011; 265.
48. V. Kandhasami Mudhaliyar, Padhinen Siddhar Aruliya Aavialikum Amudhamurai Surukkam, -Part-2, Published by Department of Indian Medicine and Homoeopathy, 2011; 286.
49. V. Kandhasami Mudhaliyar, Padhinen Siddhar Aruliya Aavialikum Amudhamurai Surukkam, -Part-2, Published by Department of Indian Medicine and Homoeopathy, 2011; 299.
50. V. Kandhasami Mudhaliyar, Padhinen Siddhar Aruliya Aavialikum Amudhamurai Surukkam, -Part-2, Published by Department of Indian Medicine and Homoeopathy, 2011; 302.
51. V. Kandhasami Mudhaliyar, Padhinen Siddhar Aruliya Aavialikum Amudhamurai Surukkam, -Part-2, Published by Department of Indian Medicine and Homoeopathy, 2011; 309.
52. V. Kandhasami Mudhaliyar, Padhinen Siddhar Aruliya Aavialikum Amudhamurai Surukkam, -Part-

2, Published by Department of Indian Medicine and Homoeopathy, 2011; 312.
53. V. Kandhasami Mudhaliyar, Padhinen Siddhar Aruliya Aavialikum Amudhamurai Surukkam, -Part-2, Published by Department of Indian Medicine and Homoeopathy, 2011; 324.
54. V. Kandhasami Mudhaliyar, Padhinen Siddhar Aruliya Aavialikum Amudhamurai Surukkam, -Part-2, Published by Department of Indian Medicine and Homoeopathy, 2011; 359.
55. Kuppusamy Mudhaliar KN, Utthamarayan KS. Siddha Vaithiya Thirattu, Published by Department of Indian Medicine & Homeopathy, Chennai, India, 1998; 63.
56. Kuppusamy Mudhaliar KN, Utthamarayan KS. Siddha Vaithiya Thirattu, Published by Department of Indian Medicine & Homeopathy, Chennai, India, 1998; 65.
57. Kuppusamy Mudhaliar KN, Utthamarayan KS. Siddha Vaithiya Thirattu, Published by Department of Indian Medicine & Homeopathy, Chennai, India, 1998; 96.
58. Kuppusamy Mudhaliar KN, Utthamarayan KS. Siddha Vaithiya Thirattu, Published by Department of Indian Medicine & Homeopathy, Chennai, India, 1998; 112.
59. Kuppusamy Mudhaliar KN, Utthamarayan KS. Siddha Vaithiya Thirattu, Published by Department of Indian Medicine & Homeopathy, Chennai, India, 1998; 120.
60. Kuppusamy Mudhaliar KN, Utthamarayan KS. Siddha Vaithiya Thirattu, Published by Department of Indian Medicine & Homeopathy, Chennai, India, 1998; 157.