Research Article

Vigna Mungo Mucilage - A Natural Polymer in the Design of Matrix Based SR Tablet of Aceclofenac

Basappa Veerabhadraiah Basavaraj*[1], Naramsetty Saritha[1], Srinivasan Bharath[1], Rajamanickam Deveswaran[1], Varadharajan Madhavan[2]
*[1]Department of pharmaceutics, [2]Department of pharmacognosy, M.S.Ramaiah College of Pharmacy, M.S.R. Nagar, M.S.R.I.T. Post, Bangalore, India.
***Corresponding author's E-mail:** bvbasu@rediffmail.com

Accepted on: 09-05-2013; **Finalized on:** 31-07-2013.

ABSTRACT

The present work reports extraction of mucilage from seed flour of *Vigna mungo* (Black gram). Physiochemical characterisation for the extracted mucilage such as phytochemical tests, Melting point, P^H, Mucilage powder flow properties along with Loss on drying were carried out. FTIR studies revealed that there was no possible drug-mucilage interaction. The seed mucilage of *Vigna mungo* has been evaluated for its matrix forming release retardant property in tablets using Aceclofenac as a model drug. The seed mucilage of *Vigna mungo* was used in 4 different concentrations of 2.5, 5, 7.5 and 10 % w/w of total weight of tablet as a release retardant. The granules were prepared by wet granulation technique and subjected to pre compression studies followed by compression. The prepared tablets were evaluated for post compression parameters and *in-vitro* dissolution profiles in comparison to marketed product. All the formulations results showed compliance with Pharmacopoeial standards. Among all the formulations V-1 (2.5 % w/w) showed sustained drug release of 82.52 % and V-4 (10% w/w) showed 29.43 % for 8 h when compared to marketed product which showed 84.24 % at the end of 8 h. The kinetic treatment showed that the mechanism of drug release from V-1 (2.5 % w/w) and V-3 (7.5 % w/w) followed diffusion whereas from formulations V-2 (5 % w/w) and V-4 (10 % w/w) it was by super case II transport .From the results obtained it is concluded that *Vigna mungo* seed flour mucilage posses good matrix forming property that could be employed in the formulation of sustained drug delivery.

Keywords: Aceclofenac, *In vitro* drug release, *Vigna mungo*(Black gram), Wet granulation technique.

INTRODUCTION

In recent years, plant mucilage have evoked tremendous interest due to their diverse applications in pharmacy, for formulation of solid dosage forms. Mucilages are pharmaceutically important polysaccharides with wide range of applications such as release retardants, binding, disintegrating, suspending, gelling, emulsifying, stabilizing agents and also as thickening agents. Binders from natural sources do hold advantages over the synthetic excipients, because of its inertness, cost, and availability. With the increase in demand for natural mucilage, it has become necessary to isolate and evaluate the newer sources of mucilage to meet the needs.[1,2]

Aceclofenac is a nonsteroidal anti-inflammatory drug (NSAID) with analgesic property used to treat pain, dysmenorrhoeal, occular inflammation, osteoarthritis, rheumatoid arthritis, etc. Due to short half life and multiple dosing regimens, aceclofenac requires sustained release formulation for patient compliance.[3] The present study was undertaken to isolate natural mucilage from Vigna mungo seeds (black gram) which can be used as an effective release retardant in pharmaceutical formulations especially as matrix tablets.[7]

MATERIALS AND METHODS

Materials

Aceclofenac is purchased from Yarrow chemicals Pvt.Ltd, Mumbai. Microcrystalline cellulose, Magnesium stearate and purified talc were purchased from S.D. Fine chemicals, Mumbai, India. *Vigna mungo* seeds (black gram) were purchased from local market, Bangalore. Isopropyl alcohol and Acetone were purchased from Central Drug House, Mumbai. All other chemicals used were of A.R grade.

Methods

Isolation of mucilage

Vigna mungo(black gram) seeds was pulverised in a hammer mill , the flour obtained was soaked in a solution of 1 % w/v of sodium meta bisulphite solution for 24 h and passed through muslin cloth, the filtrate was desolvated with acetone in the ratio of 1:2. The obtained product was dried in oven at 50°C for 6-8 h. The dried product was finally powdered and passed through sieve 80 and stored for further use.

Formulation of Aceclofenac matrix tablets

Procedure for preparation of matrix tablets

Aceclofenac SR- matrix tablets were prepared by wet granulation technique using varying concentrations of *Vigna mungo* seed mucilage as matrix forming material and isopropyl alcohol as binding agent as mentioned in Table 1. To the mucilage powder Aceclofenac and, microcrystalline cellulose were added and triturated to form a uniform blend. The powdered blend then subjected to granulation by using isopropyl alcohol as granulating agent. The wet mass was passed through sieve no. 12 and the granules obtained were dried at 45^{0}C for 30 min. The dried granules were passed through sieve no.16 and lubricated with magnesium stearate and talc.

The blended granules were finally compressed in to tablets of desired weight (300mg) and hardness by using 8 mm concave punch in rotary tablet press (Rimek RSB-4 minipress, Cadmach).

Evaluation Studies

Physicochemical properties and characterization of mucilage of *Vigna mungo*[6]

Phytochemical examination

Ruthenium red test, Molisch's test and Iodine test was performed to confirm the presence of polysaccharide.

Molisch's test

The sample was treated with alcoholic solution of α - Naphthol and a few drops of conc. sulphuric acid were added through the sides of the test tube. The formation of violet ring at the junction of the liquids indicates the presence of carbohydrates.

Ruthenium red test

To the mucilage solution ruthenium red reagent was added, appearance of pink colour indicates presence of mucilage.

Iodine test

To the mucilage solution iodine solution was added, appearance of reddish brown colour indicates presence of carbohydrates.

Micromeritic properties of Vigna mungo seed mucilage

Bulk density, tap density, bulkiness, angle of repose, Hausner's ratio and carr's index was determined.

Loss on drying (LOD)

0.5 g of mucilage powder was weighed and placed in a clean and dry weighing bottle. It was kept in hot air oven at 105° C for 5 h. The bottle was removed from the oven and cooled. Then the weight of the mucilage powder was determined. Loss on drying was calculated by the following equation

% LOD = initial weight – final weight / initial weight X 100

pH of 1% solution

The pH of the *Vigna mungo* seed mucilage solution was measured using a digital pH meter by dispersing 0.5 g of mucilage powder in 50 ml of distilled water.

Drug- polymer compatibility studies

Drug- polymer compatibility studies were carried out using Fourier Transform Infrared Spectrophotometer (Shimadzu FT-IR 8400-S) by KBr disc method. A small amount of drug was mixed with the Spectroscopic grade of KBr and triturated for uniform mixing. The thin and transparent palate is prepared by applying 2000 psi pressure. The prepared palate is exposed to the IR beam and spectra are recorded by using FTIR 8400 Shimadzu, Japan, by scanning in the range of 400- 4000 cm^{-1}.

Table 1: Formulation of Aceclofenac SR-matrix tablets

Ingredients	V-1	V-2	V-3	V-4
Aceclofenac (mg)	200	200	200	200
Vigna mungo mucilage powder (%w/w)	2.5	5	7.5	10
Microcrystalline cellulose (mg)	84.5	77	69.5	62
Talc (mg)	5	5	5	5
Magnesium stearate (mg)	3	3	3	3
Isopropyl alcohol (ml)	q.s to 300mg	q.s to 300mg	q.s to 300mg	q.s to 300mg

Pre compression studies[5]

a) Angle of repose

Procedure

Fixed funnel method was used. A funnel was fixed with its tip at a given height (h) of about 2 cm, above a flat horizontal surface on which a graph paper was placed. The powder (10 g) was taken in the funnel and the test sample was allowed to flow smoothly, till the apex of the conical pile just touches the tip of funnel. The height and diameter of the powder cone was measured and angle of repose (θ) was calculated by using the following equation,

$$\tan \theta = h / r$$

Where, θ = angle of repose; h = height of the heap of powder; r = radius of the base of the powder.

Table 2: Limits for angle of repose

Flow Property	Angle of Repose (degrees)
Excellent	25–30
Good	31–35
Fair—aid not needed	36–40
Passable—may hang up	41–45
Poor—must agitate, vibrate	46–55
Very poor	56–65
Very, very poor	>66

b) Bulk density (D_b)

Procedure

Bulk density was determined by taking accurately weighed quantity of the dried granules in a measuring

cylinder and recording the volume and weight of the total granules. It is expressed in gm/ml and is given by,

$D_b = M / V_o$

Where, D_b = Bulk density (g/ml); M = weight of granules (g); V_o = bulk volume of granules (ml)

c) *Tapped density (D_t)*

Procedure

Tapped density was determined (Tapped density apparatus, Electrolab, ETD-1020, India) by taking accurately weighed quantity of the dried granules in a measuring cylinder and recording the volume of granules after 100 tapping and weight of the total granules. It is expressed in g/ml and is given by,

$D_t = M / V$

Where, D_t = Tapped density (g/ml), M = weight of granules (g), V = tapped volume of granules (ml)

d) Carr's Index

Carr's Index is an important measure that can be obtained from the bulk and tapped densities. In theory, the less compressible a material the more flow able it is. A material having values of less than 20 is defined as the free flowing material (Table 3). The formula for Carr's Index is as follows

$$\text{Carr's Index (\%)} = \frac{(Dt - Db)}{Dt} \times 100$$

Table 3: Scale of Flowability

Compressibility Index (%)	Flow Character	Hausner's Ratio
10	Excellent	1.00–1.11
11–15	Good	1.12–1.18
16–20	Fair	1.19–1.25
21–25	Passable	1.26–1.34
26–31	Poor	1.35–1.45
32–37	Very poor	1.46–1.59
>38	Very, very poor	>1.60

e) Hausner's ratio

It indicates the flow properties of the powder and is measured by the ratio of tapped density to the bulk density.

Hausner's ratio = (Tapped density)/ (Bulk density)

Post compression studies

The prepared tablets were evaluated for weight variation test, hardness, disintegration time and friability.[5]

a. Weight variation test

The tablet designed to contain a specific amount of polymer in a specific amount of tablet formula, the weight of the tablet being made is routinely measured to ensure that a tablet contains the proper amount of polymer. The IP weight variation test was done by weighing 20 tablets individually, calculating the average weight and comparing the individual weights to the average. The tablet meet the IP test if no more than 2 tablets are outside the percentage limits. IP official limits of percentage deviation of tablet are presented in the Table 4.

Table 4: Limits for weight variation test

Average weight of tablet (mg)	Maximum % difference allowed
≤ 80 mg	10
80-250 mg	7.5
≥ 250 mg	5

b. Hardness

The resistance of tablets to capping, abrasion or breakage under conditions of storage, transportation and handling before usage depends on its hardness. The instrument measures the force required to break the tablet when the force generated by anvils to the tablet. Tablet hardness is defined as the load required crushing or fracture a tablet placed on its edge. Sometime it is also termed as tablet crushing strength. The hardness of the tablets was determined using Monsanto hardness tester. It is expressed in kg/cm^2. Three tablets were randomly picked and hardness of the tablets was determined.

c. Friability Test

Friability generally refers to loss in weight of tablets in the containers due to removal of fines from the tablet surface. Friability generally reflects poor cohesion of tablet ingredients.

Method

10 tablets were weighed, initial weight of these tablets were recorded and placed in Roche friabilator and rotated at the speed of 25 rpm for 100 revolutions. Then tablets were removed from the friabilator, dusted off the fines and again weighed and the weight was recorded.

Percentage friability was calculated by using the formula;

$$\% \text{ friability} = \frac{Initial\ weight\ of\ tablets - Final\ weight\ of\ tablets}{Initial\ weight\ of\ tablets} \times 100$$

Drug content determination

Drug content was determined at 277 nm by UV-Visible spectrophotometer (UV-1601, Shimadzu) using 7.4 pH buffer as blank.

***In-vitro* drug release**

In-vitro drug release was studied using dissolution test apparatus USP type II method (rotating paddle method). The formulated tablet dosage forms were introduced into dissolution flasks containing 900 ml of 0.1N HCl. The temperature was maintained at 37±0.5 ºC and basket rotated at 50 rpm. 2 ml of aliquot was withdrawn at regular predetermined intervals and sink conditions were

maintained throughout the study by replacing equal volume of fresh dissolution medium. After 2 h, dissolution medium was replaced with pH 7.4 phosphate buffer and dissolution study was carried out. The samples taken were diluted to 25 ml with distilled water and analyzed spectrophotometrically at 277 nm using distilled water as blank. All the analysis was carried out in triplicate.

In-vitro drug release mechanism

In-vitro release mechanism was determined by using PCP DISSO V3 software. To analyze the in vitro release data various kinetic models such as zero order, 1st order, Hixson-Crowell cube root law, Peppas model and Higuchi model were used to describe the release kinetics. Based on this the following plots were made: cumulative % drug release vs. time(zero order kinetic model); cumulative % drug release Vs log time (Korsmeyer model) and cube root of drug % remaining in matrix vs. time(Hixson-Crowell cube root law). To find out the mechanism of drug release, first 60% drug release data was fitted in Korsmeyer- Peppas model:

$$M_t / M_\infty = K_t^n$$

Where M_t / M_∞ is the fraction of drug released at time t, K is the rate constant and n is the release exponent. Then n value is used to characterise different release mechanisms.[4]

RESULTS AND DISCUSSION

Physicochemical properties and characterization of mucilage of *Vigna mungo*

a) Phytochemical examination

Ruthenium red test, Molisch's test and Iodine test were performed to confirm the presence of polysaccharide.

b) Micromeritic properties of Vigna mungo seed mucilage

Bulk density, tap density, bulkiness, angle of repose, Hausner's ratio and carr's index were determined.

c) Loss on drying (LOD)

LOD was carried out as per method mentioned in IP 2007.

d) pH of 1% solution

The pH was measured using a digital meter.

The % yeild of *Vigna mungo* seed mucilage was 52%. The identification of polysaccharide was comfirmed by ruthenium red test as it stained red in colour, and the presence of carbohydrates was confirmed by Molisch's test as there was formation of violet ring at the junction of the liquids. The results of the micromeritic properties of isolated *Vigna mungo* seed mucilage powder were shown in table 5. The values of bulk density, tap density of *Vigna mungo* mucilage powder were 0.5 g/cc, 0.55 g/cc. The value of angle of repose was found to be $31^0 80'$ indicating good flow properties. This was further supported by Carr's index and Hausner's ratio values which were found to be 9.09, 1.1 respectively showing excellent flow characteristics.

2. Drug- polymer compatibility studies

The compatability between the drug and isolated *Vigna mungo* seed mucilage powder was found to be good as confirmed by I.R spectral studies. The infra red spectra of pure Aceclofenac showed peaks at 1681.81cm^{-1}, 3118.68 cm^{-1}, 3388.70 cm^{-1}, 1651.12 cm^{-1}, 781.12 cm^{-1} and 1716.53 cm^{-1} confirming the presence of -COOH stretch, -CH stretch (aromatic), - NH stretch, C=O stretch, C-Cl and C-O stretch respectivelyas shown in figure 1a. The spectra of physical mixtures *vigna mungo* seed mucilage powder and aceclofenac showed similar peaks at their respective wave numbers (Figure 2c). This part of the study confirmed that there was no interaction between drug and *vigna mungo* seed mucilage powder.

Table 5: Physicochemical properties and characterization of *vigna mungo* seed mucilage

Parameters		Results
Melting point		118-220°C
Loss on drying		6%
Angle of repose		$31^0 80'$
Bulk density(g/cc)		0.5
Tapped density (g/cc)		0.55
Carr's index		9.09
Hausner's ratio		1.1
P^H of 1% mucilage solution		7.0
Phyto chemical tests for identification of presence of mucilage	a. Ruthenium red test	+
	b. Molisch test	+
	c. Iodine test	+

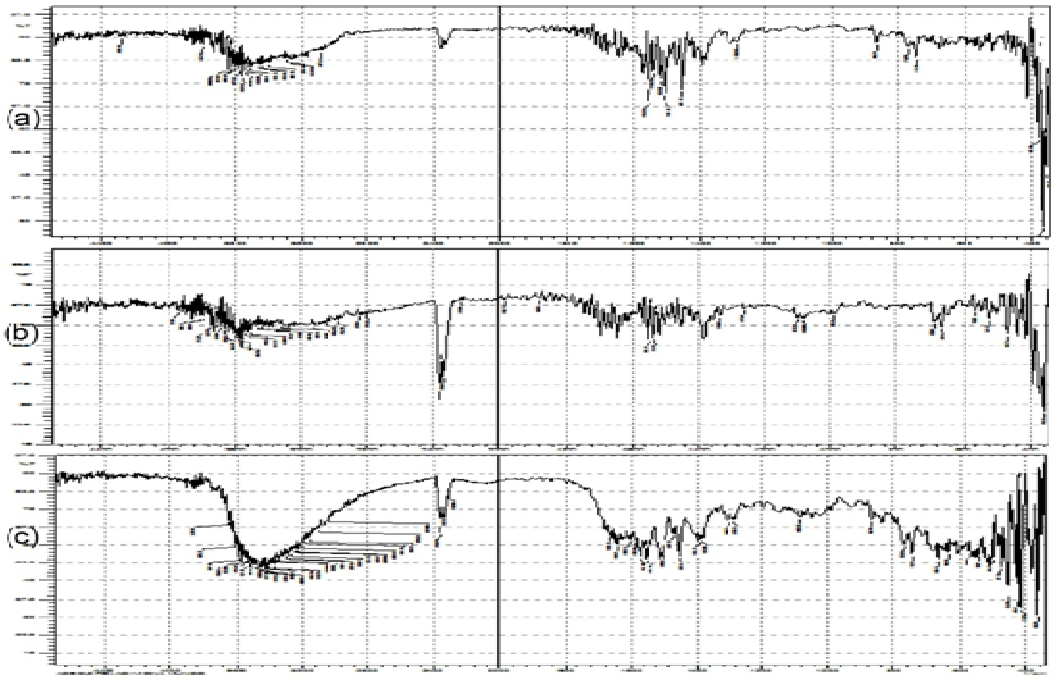

Figure 1: IR spectra of (a) Aceclofenac; (b) *Vigna mungo* mucilage powder; (c) Physical mixture of Aceclofenac and *Vigna mungo* mucilage powder.

Pre compression studies

Table 6: Pre compression parameters of formulation granules

PARAMETERS		V-1	V-2	V-3	V-4
Wt. of the granules(g)		2.98	3	2.95	2.83
Bulk density(g/ml)		0.39	0.428	0.42	0.377
Tapped density(g/ml)		0.45	0.5	0.53	0.471
Compressibility index(%)		13.33	16	20.7	21.27
Hausners ratio		1.15	1.19	1.26	1.24
Angle of repose	with glidants	$23^0 74'$	$23^0 96'$	$24^0 94'$	$23^0 19'$
	without glidants	$21^0 80'$	$22^0 71'$	$22^0 71'$	$21^0 31'$

Post compression studies

Table 7: Post compression Studies

PARAMETERS	V-1	V-2	V-3	V-4
Weight variation (%)	0.29±0.02	0.30±0.01	0.28±0.02	0.29±0.02
Thickness(mm)	3	3	3	3
Friability (%)	0.48	0.49	0.49	0.5
Hardness(kg/cm^2)	5	5.5	5.5	5
Drug content (%)	96.8	99.3	96.5	98
Disintegration time (hr: min : sec)	20	1:20	1	1:5

Table 8 : *In vitro* drug release kinetics of formulations

Formulation Code	Zero Order		First Order		Matrix		Hixon Crowell		Korsemeyer-Peppas		
	R^2	K	R^2	K	R^2	K	R^2	K	R^2	K	n
V-1	0.9831	7.6338	0.9350	0.1100	0.8877	17.61	0.9552	0.0322	**0.9835**	7.3906	0.9940
V-2	**0.9834**	5.6519	0.9586	0.0718	0.8810	13.0006	0.9683	0.0220	0.9750	5.3240	1.0005
V-3	0.9783	4.5748	0.9538	0.0552	0.8731	10.5038	0.9630	0.0172	**0.9914**	3.7985	1.0791
V-4	**0.9954**	3.1800	0.9935	0.0356	0.9214	7.4013	0.9944	0.0114	0.9888	2.3376	1.1856

Aceclofenac SR- Matrix tablets were formulated by using *vigna mungo* seed mucilage powder as polymer as mentioned in Table 1. with varying concentrations of mucilage powder. The prepared tablets complied with the pharmacopoeial specifications for weight variation test, hardness and friability of less than 1%, thereby substantiating the mechanical resistance of the tablets during transit.The drug content of all the tablets was found to be in the range of 96.5 to 99.3%. Table 7 gives the physical parameters (hardness, thickness and friability), weight uniformity , disintegration time and drug content of all the fabricated tablets.

In-vitro drug release studies

The *in-vitro* drug release studies revealed that the formulation V-4 containing maximum concentration of mucilage showed a slow and sustained drug release of 29.43 % at the end of 8h when compared to 88 % of drug release from the marketed product. The results indicated that as the concentration of *Vigna mungo* mucilage was increased the drug release rate was retarded.

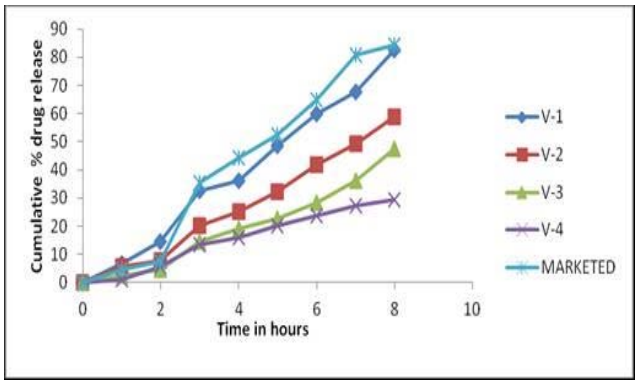

Figure 2: Comparative *in vitro* dissolution profile of the prepared formulations and marketed product

In vitro drug release kinetics

The dissolution data of all the batches were fitted to first order, Higuchi, Zero order and Korsmeyer- peppas models. The model that best fitted the release data was evaluated by correlation coefficient (r^2); the values for all formulations in various models are given in Table 8. The release mechanism for formulations V-1 (n-value: 0.9940-anamolous diffusion) and V-3 (n-value: 1.0791-supercase II transport) was found to be by peppas model with r^2 value of 0.9835 and 0.9914 respectively. The predicted drug release mechanism would be diffusion process. similarly for V-2(n-value:1.005-supercase II transport) and V-4(n-value:1.1856-supercase II transport) the best fit model was found to be Zero order kinetics with r^2 value of 0.9834 and 0.9954 respectively indicating super case II type transport. The r^2 values of all the formulations confirmed that the drug release mechanism from the formulated tablets was diffusion controlled.

CONCLUSION

Mucilage was isolated from the seeds of *Vigna mungo* and studied for its release retardant property. The isolated mucilage was subjected to various physic chemical studies and found that it was stable and suitable as a formulation additive. The mucilage powder with the maximum concentration of 10 % w/w showed sustained drug release of 29.43 % at the end of 8h showing good sustained release and matrix forming capacity. Thus it can be concluded that the mucilage from the natural source in suitable concentration could be employed in the development of sustained release tablets and its other pharmaceutical applications needs to be explored.

Acknowledgement: The material assistance and moral support from the GEF (Medical) in the smooth completion of research work is profoundly acknowledged.

REFERENCES

1. Sravani B, Deveswaran R, Bharath S, Basavaraj BV, Madhavan V, Studies on *Vigna mungo* seed mucilage as a pharmaceutical excipient, Journal of Chemical and Pharmaceutical Research, 3(2), 2011, 118-125.
2. Yadav IK, Jaiswal D, Ghosh N, Singh HP, Mishra A, Bhattacharya A, Bajpai M, Evaluation of seed flour of *vigna mungo* (L) based sustained release matrix tablets of Diclofenac sodium, Journal of Pharmacy Research, 2(5), 2009, 834-838.
3. Tripathi KD, Essentials of medical pharmacology, 5th ed, Jaypee Brothers Medical Publishers, New Delhi, 2003.
4. Najib N, Suleiman M, The kinetics of drug release from ethyl cellulose solid dispersions, Drug Development and industrial Pharmacy, 11, 1985, 2169–2181.
5. The United State Pharmacopoeia, 26th ed. Port City Press, USA, 1, 2008, 639-641.
6. Anusha putteti, Isolation, characterization and formulation properties of a mucilage obtained from *Plantago ovata(dissertation),* Rajiv Gandhi university of health sciences, 2011, 91-101.
7. Subramaniam kannan, Rangasamy Manivannan, Kugalur Ganesan, Prathiban Kakkatummal nishad, Natesan Senthil kumar, Formulation and Evaluation of sustained release tablets of aceclofenac using hydrophilic matrix system, International Journal of Pharm Tech research, 2, 2010, 1775-1780.

Source of Support: Nil, **Conflict of Interest:** None.