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FORMULATION, DEVELOPMENT AND EVALUATION OF TABLET CONTAINING PLANT EXTRACTS OF MOMORDICA DIOICA AND MONOCHORIA VAGINALIS

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ABSTRACT

Plant-derived drugs are desired for anticancer treatment as they are natural and readily available.Being naturally derived compounds from plants they are generally more tolerated and non-toxic to normal human cells.Momordica dioica and Monochoria vaginalis are the anticancer drugs used in the treatment of breast cancer. Herbal tablets of extract of Momordica dioica and Monochoria vaginalis were formulated and evaluated for anti-cancer activity. Herbal tablets were evaluated by various post compression parameters like hardness, thickness, friability, dispersion time, wetting time, % moisture uptake study, water absorption study, disintegration time and in vitro dissolution rate. In vitro cytotoxicity study of paclitaxel, combination of Monochoria vaginalis and Momordica dioica against MDA-MB-231 & MDA-MB-231-DR cell lines was assessed after 72 hrs of incubation by MTT assay. This showed potent anticancer activity of Momordica dioica and Monochoria vaginalis for the treatment of breast cancer.

INTRODUCTION

Herbal drugs are the medicines obtained from the plants, parts of plants and isolated phytochemicals. Their use for the prevention and treatment of various health ailments has been in practice from time immemorial. Herbal medicines contain more than one active compound. Generally they are not completely free from side effects but the risk associated with herbal drugs is very less. They have distinctive characteristics that make them different from synthetic drugs.[1] Plant-derived drugs are desired for anticancer treatment as they are natural and readily available. They are being investigated for their ability to inhibit growth and initiate apoptosis of cancerous cells.[2] Momordica dioica and Monochoria vaginalis are the anticancer drugs used in the treatment of breast cancer. Herbal tablet of extract of Momordica dioica and Monochoria vaginalis were formulated and evaluated for anti-cancer activity. It is considered most natural, uncomplicated, convenient, safe means of administrating drugs, greater flexibility in dosage form design, ease of production, versatile, flexible in dosage strength, relatively stable, present lesser problem in formulation, packaging and it is convenient to manufacture, store, handle and use. In vitro cytotoxicity study of paclitaxel, combination of Monochoria vaginalis and Momordica dioica against MDA-MB-231 & MDA-MB-231-DR cell lines was assessed after 72 hrs of incubation by MTT assay. This showed potent anticancer activity of Momordica dioica and Monochoria vaginalis for the treatment of breast cancer.

MATERIALS AND METHODS: Roots of Momordica dioica and stems & leaves of

Monochoria vaginalis were collected from rural areas of Gondia district in Maharashtra state and extracted in college laboratory. Chloroform, Petroleum ether, Ethyl acetate, ethanol, n-hexane, methanol, Microcrystalline cellulose, Magnesium stearate, Talc, Dibasic calcium phosphate, potassium dihydrogen phosphate, disodium hydrogen phosphate and sodium chloride were obtained from Loba Chemicals Pvt. Ltd., Mumbai, India. Acetone was obtained from Merck Specialities Pvt. Ltd. Mumbai. Other chemicals used in the study were of analytical grade.

FORMULATION OF TABLET

Direct Compression Method: Herbal tablets were prepared by direct compression method. All the Formulation ingredients mentioned in table no.1 were weighed accordingly and mixed in a mortar and pestle. This powder blend was then allowed to dry for few moments and then again mixed well and passed through sieve no. 60. Blend was compressed by punching machine (Model: Rimek – mini press-1).[3,4]

Thin Layer Chromatography Study [5,6,7,8,9,10]

Active extracts those having promising anticancer activity were subjected to thin layer chromatography to find out the number of compounds present in them

Antimitotic Activity[11]: The antimitotic activity was screened using Allium cepa root meristematic cells which have been used extensively in screening of drug with antimitotic activity. Cells of this region undergo repeated divisions, known as meristematic region, which is similar to cancer division in humans. Hence Allium cepa meristematic cells can be used for preliminary screening of drug with anticancer activity.

Cytotoxicity Study: The cytotoxicity study of drug extracts and paclitaxel was evaluated using the MTT assay. In short, MBA-MD-231 (3×103 cells/well) and MBA-MD-231 DR (3×103 cells/well) cells were moved to 96-well tissue culture plates. After 24 h, the medium was removed and replaced with fresh medium containing PTX, Momordica dioica, Monochoria vaginalis and combination of MD & MV at different concentrations. Control wells had only fresh culture media. The 96-well plates were incubated for 72 h at 37°C and 5% CO_2. Then, the medium was removed and cells in each well were gently washed twice with sterile PBS (1X). Fifty (50) μL of MTT solution (0.5 mg/mL) was added to each well and again incubated for 4 h at 37°C and 5% CO_2. After 4 h, the medium was removed and 100 μL of DMSO was added to each well to dissolve the purple formazan crystals. Viability of the cells was determined by measurement of the absorbance at 570 nm by a microplate reader(Varioskan Flash). The percentage cell viability with different treatments was determined.[12]

EVALUATION OF TABLET[3,13]

Precompressional Studies of Tablet Blend

In development of new dosage form preformulation study is the prior step in the potential drug development. It is the principal investigation in the drug development to obtained information on the known properties of compound and the proposed development schedule. So, this preformulation investigation may merely confirm that there are no significant barriers to compound development. Following pre-compressional parameters were studied like angle of repose, bulk density, tapped density, compressibility indices etc.

Angle of repose: It is the maximum angle that can be obtained between the freestanding surface of powder heap and the horizontal plane. It was determined by using fixed funnel method. Specified amount of powder drug was transfer to the funnel keeping the orifice of the funnel blocked by thumb. When powder was cleared from funnel then measured its angle of repose and measured in θ.

$$\text{Angle of repose } (\theta) = \tan^{-1} h/r$$

Bulk density: It is the ratio of bulk mass of powder to the bulk volume. It is denoted by ρb. Bulk density is used to find out homogenecity.

$$\text{Bulk density } (\rho b) = M/Vb$$

Where, M is the mass of the sample, Vb is the bulk volume

Tapped density: It is the ratio of the weight of powder to the minimum volume occupied in

measuring cylinder. Tapped density is determined by placing a graduated cylinder containing a known mass of drug or formulation on a mechanical tapper apparatus which is operated at fixed no. of taps (1000) until the powder bed reached a minimum volume.

Tapped density (ρt) = weight of powder blend/Minimum volume occupied by cylinder

Compressibility Indices

a. Carr's index: Based on the apparent bulk density and the tapped density, the percentage compressibility of the powder mixture was determined by the following formula.

Carr's index = Tapped density-Bulk density × 100/ Tapped Density

b. Hausner's ratio: It is an indirect index of ease of measuring of powder flow. Lower Hausner's ratio (<1.25) indicates better flow properties than higher ones (>1.25).

Hausner's ratio = Tapped density/ Bulk density

POST-COMPRESSIONAL STUDIES OF PREPARED TABLETS

The tablets were evaluated for various parameters after consideration of preformulation to overcome errors during formulation preparation. These are like appearance, thickness, weight variation, hardness, disintegration study, drug content and in vitro drug release.

Physical appearance: The general appearance of tablet was studies visually in shape, color, texture and odour.

Thickness: The tablet thickness was calculated by Vernier callipers. Tablet was put in between two jaws vertically and measured thickness and 6 tablets were used for this test and expressed in mm.

Weight variation: Weight variation test is run by weighing 20 tablets individually, calculating the average weight and comparing individual tablet weight to the average. The weight variation test would be a satisfactory method of determining the drug content uniformity of tablets.

Hardness: Hardness also termed as tablet crushing strength. The tablet hardness was determined by Monsanto hardness tester (Model: THERMONIK-campbell electronic). The tablet was placed lengthwise between upper and lower plunger and force applied by turning a threaded bolt until the tablet fractures and measured hardness of tablet in Kg/cm^2.

Friability: It is determined by Roche friabilator(Model: Electrolab-(USP) EF-1W), subjects a number of tablets to combined effects of abrasion and shock by utilising a plastic chamber that revolves at 25 rpm, dropping tablet from inches distance operated for 100 revolutions. Pre-weighed tablets were dusted and re-weighed and according to standard limit friability should be less than 1%. It is calculated by formula-

% Friability = Initial weight – Final weight / Initial weight *100

Wetting time: A piece of tissue paper folded twice was placed in a small petridish containing 6ml of water. A tablet was kept on the paper and time required for complete wetting was measured. The wetted tablet was then weighed.

Water absorption ratio: A piece of tissue paper folded twice was placed in a small petridish containing 6ml of water. A tablet was placed on the paper and time required for complete wetting was measured. The water absorption ratio (R) was determined using the following equation.

R= (Wa-Wb)/Wb X 100

Where, Wa is the weight of the tablet after water absorption, Wb is the weight of the tablet before water absorption

Moisture uptake studies: Several oral dosage forms are hygroscopic and cannot maintain physical integrity under normal condition of temperature and humidity which calls for specialized product packaging.

Table no. 1: Formulation of tablets

Sr no.	Name of ingredient	Formulation code (quantity in mg)			
		F1	F2	F3	F4
1	Momordica dioica	50	50	50	50
2	Monochoria vaginalis	50	50	50	50
3	Micro crystalline cellulose	135	150	165	180
4	Dicalcium phosphate	62.75	47.75	30	17.75
5	Magnesium stearate	1.125	1.125	1.125	1.125
6	Talc	1.125	1.125	1.125	1.125

A **B**

Fig no. 1: Thin Layer Chromatography of **A**. *Monochoria vaginalis*, **B**. *Momordica dioica* extract.

Table no. 2 : Results of preliminary phytochemical screening of ethanolic extracts of Momordica dioica and Monochoria vaginalis

Tests	Test performed and reagents	Momordica dioica	Monochoria vaginalis
Test for Sterols	Salkowaski Reaction	+++	+++
	Liebermann's Reaction	+++	+++
	Liebermann-Burchard Reaction	+++	+++
Test for Alkaloids	Dragendorff's Reagent	++	+++
	Mayer's Reagent	---	---
	Wagner's Reagent	---	---
	Hager's Reagent	+++	++
Test for Saponins	Foam Test	---	---
Test for Sugars	Molish Test	++	++
	Barfoed Test	---	---
	Fehling solution Test	+++	+++
Test for Flavonoids	Shinoda test	++	++
Test for Proteins	Biuret Test	+++	++

Tests	Test performed and reagents	Momordica dioica	Monochoria vaginalis
	Xanthoprotic Test	---	---
Test for Tannins	$Fecl_3$ Solution	+++	+++
	Lead Acetate solution	---	---
	Pot. Dichromate Solution	+++	++
Test for Amino Acids	Ninhydrin Test	+++	+++
Test for triterpenois	Salkowski test	+++	+++
	Libermann-Burchard test	+++	+++
Coumarins	-----	---	---
Cardiac glycosides	Killer Killani test	+++	+++
	Legal test	---	---
	Baljet test	---	---
Anthroquinone glycosides	Borntrager test	---	---
Cyanogenetic glycosides	Grignard test	---	---

+++ = Present, --- = Absent

THIN LAYER CHROMATOGRAPHY OF MOMORDICA DIOICA AND MONOCHORIA VAGINALIS

Spots were detected using UV light (UV Chamber) and spraying (50%) H_2SO_4.

Table no. 3 : TLC R_f value of Momordica dioica and Monochoria vaginalis

Drug	Solvent system used	No of spot	Distance travelled by solute	Distance traveled by solvent front	R_f value
Momordica dioica	Benzene	3	1.2 2.9 5.1	5.8 5.8 5.8	0.2 0.5 0.8
Monochoria vaginalis	Benzene	3	1.3 2.5 5.2	5.6 5.6 5.6	0.2 0.4 0.9

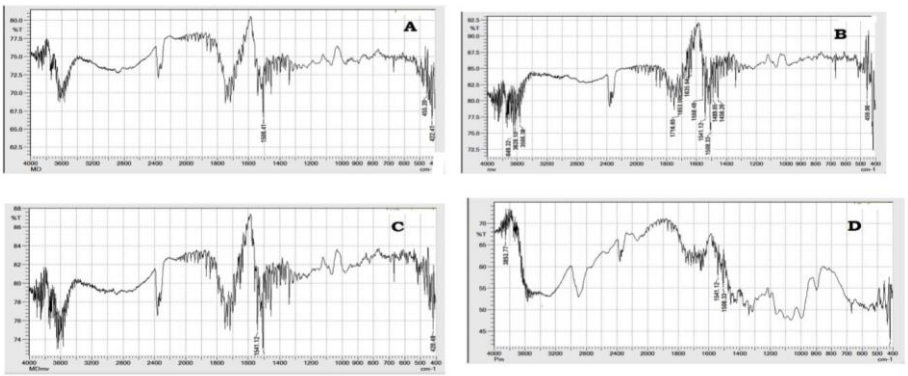


Fig. no. 2 : FTIR spectrum of **A**. plant extract of MD, **B.** plant extract of MV, **C.** combination of MD & MV, **D.** physical mixture of extracts with excipients

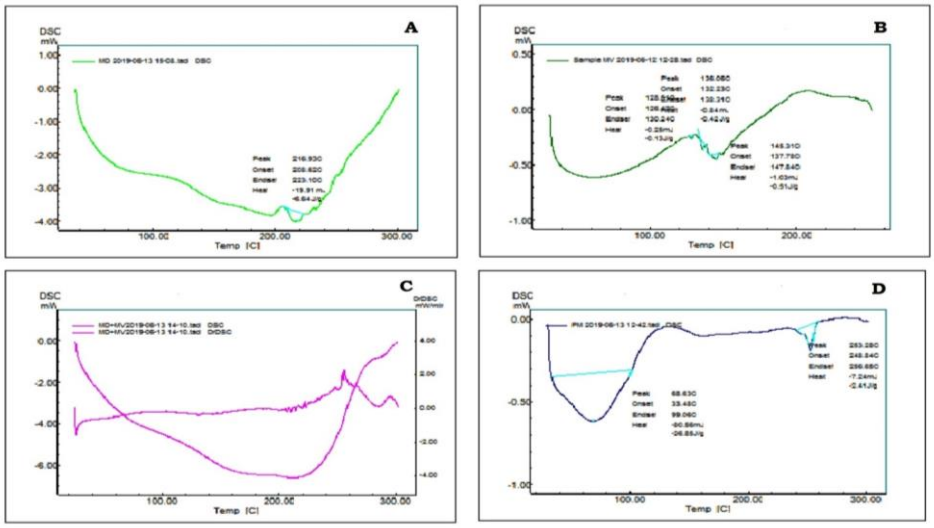
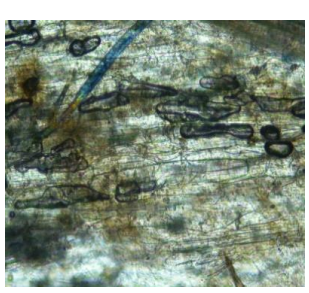
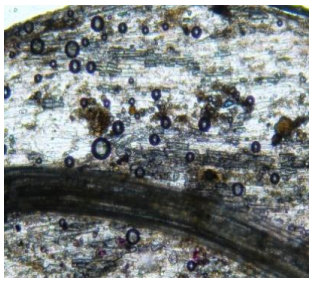


Fig. no. 3 : DSC thermograms of **A**. plant extract of MD, **B.** plant extract of MV, **C.** combination of MD & MV, **D.** physical mixture of extracts with excipient

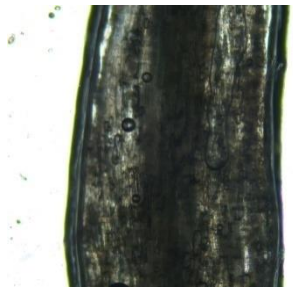
Fig no. 4 : Mitotic inhibition of Allium cepa roots attained after incubation with water, methotrexate, M. dioica, M. vaginalis and MD+MV



Water

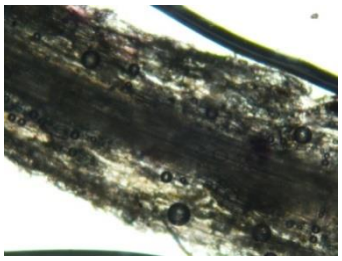


Methotrexate



M. Dioica

M. Vaginalis



MD+M.V

Table no.4: Allium cepa root length attained after incubation with water, methotrexate, M. dioica, M. vaginalis and MD+MV.

Sr no.	Sample	Root length (cm)			
		0 h	24 h	48 h	72 h
1	Water	2.68±0.15	2.98±0.25	3.35±0.65	3.68±0.98
2	Methotrexate	1.38±0.38	1.58±0.62	1.85±0.06	2.29±0.36
3	M. dioica	1.72±0.36	1.99±0.35	2.35±0.65	2.92±0.65
4	M. vaginalis	1.78±0.96	1.95±0.65	2.30±0.62	2.96±0.62
5	MD+MV	1.65±0.36	2.06±0.98	2.36±0.53	2.65±0.35

Table no. 5: Mitotic inhibition of Allium cepa roots attained after incubation with water, methotrexate, M. dioica, M. vaginalis and MD+MV.

Sr no.	Sample	Total no. of cells	No. of cells in mitosis	Mitotic index	Mitotic inhibition (%)
1	Water	40	21	52.52	0
2	Methotrexate	35	10	28.57	45.60
3	M. Dioica	25	07	28.00	46.68
4	M. Vaginalis	38	09	23.68	54.91

Table no. 6: Physical properties for tablet blend

Batch	Angle of repose (°)	Bulk density (gm/ml)	Tapped density (gm/ml)	Carr's index (%)	Hausner's ratio
F1	21.12±0.11	0.4649±0.12	0.4262±0.08	12.19±0.14	1.14±0.16
F2	24.32±0.12	0.4741±0.32	0.4132±0.17	13.04±0.16	1.16±0.021
F3	27.46±0.12	0.4541±0.21	0.4587±0.023	11.00±0.12	1.11±0.012
F4	22.14±0.17	0.407.21±0.32	0.4965±0.028	14.17±0.39	1.17±0.13

±S.D.= Standard deviation,

Table no. 7: Results for post compressional study of tablets

Batch	Hardness (kg/cm^2)	Friability (%)	Thickness (mm)	% weight variation
F1	3.92±0.95	0.48	3.11±0.36	2.32±0.63
F2	3.35±0.35	0.85	3.65±0.52	2.05±0.36
F3	3.73±0.21	0.82	3.07±0.32	1.23±0.56
F4	3.25±0.65	0.92	3.98±0.25	-1.32±0.32

±S.D.= Standard deviation, n=3

Table no. 8: Results for post compressional study of tablets

Batch	Disintegration time (sec)	Wetting time (sec)	% water absorption ratio (sec)	% moisture uptake	Dispersion time (sec)
F1	134±0.0.28	128±0.69	140±0.39	4.35±0.65	93±2.02
F2	141±0.0.35	124±0.95	168±0.36	3.25±0.62	89±0.95
F3	156±0.0.32	138±0.35	150±0.21	2.35±0.35	90±1.25
F4	145±0.2.30	129±0.08	151±0.35	2.36±0.98	95±2.50

±S.D.= Standard deviation, n=3

Table no. 9: Results for % Drug content and % Release study of tablets

Batch	% Drug content		% Drug release	
	MD	MV	MD	MV
F1	94.35±0.024	94.25±0.321	62.88 ± 1.9	59.18 ± 1.25
F2	92.36±0.154	91.35±0.045	68.88 ±1.758	64.96 ± 1.35
F3*	97.89±0.058	98.35±0.098	70.35 ± 1.25	68.68 ± 1.65
F4	102.36±0.065	103.52±0.581	59.27 ±1.235	54.10 ± 1.65

±S.D.= Standard deviation, n=3

Table no. 10: *In vitro* dissolution study for MD

Time (min)	% Drug release			
	F1	F2	F3	F4
0	0±0	0 ± 0	0 ± 0	0 ± 0
10	13.158 ±0.547	17.299 ±0.314	17.299 ±0.247	17.299 ±0.345
20	27.27 ± 0.687	31.724 ±0.654	34.896 ±0.347	30.535 ±0.547
30	39.812 ± 1.25	39.821 ±0.968	42.336 ±0.687	42.331 ±0.687
40	47.742 ±1.657	47.839 ±1.345	52.692 ±0.867	46.783 ±0.728
50	57.046 ±1.821	60.183 ±1.657	67.156 ±0.968	52.694 ±0.952
60	62.88 ± 1.9	68.885 ±1.758	70.358 ± 1.25	59.273 ±1.235

±S.D.= Standard Deviation, n=3

Table no. 11: *In vitro* dissolution study for MV

Time (min)	% Drug release			
	F1	F2	F3	F4
0	0 ± 0	0 ± 0	0 ± 0	0 ± 0
10	20.556 ±0.025	22.977 ± 0.34	23.336 ±0.358	16.722 ±0.258
20	25.732 ±0.056	27.101 ± 0.58	27.101 ±0.624	25.672 ±0.425
30	30.074 ±0.095	32.907 ±0.829	32.715 ±0.869	32.155 ±0.627
40	37.561 ±0.125	38.935 ± 0.93	43.033 ±0.954	40.603 ±0.821
50	49.538 ± 0.68	49.068 ± 1.25	50.942 ± 1.25	49.803 ± 1.53
60	59.18 ± 1.25	64.964 ± 1.35	68.686 ± 1.65	54.101 ± 1.65

±S.D.= Standard Deviation, n=3

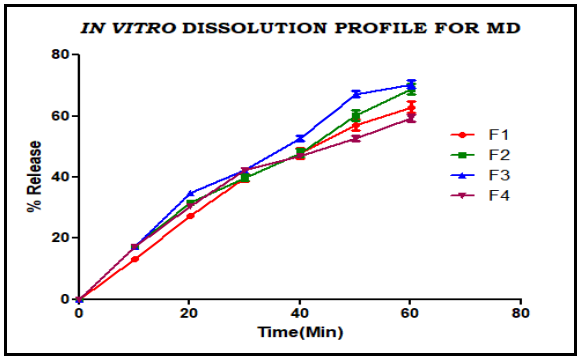


Fig no. 5: Dissolution profile of formulation from F1-F4 for MD

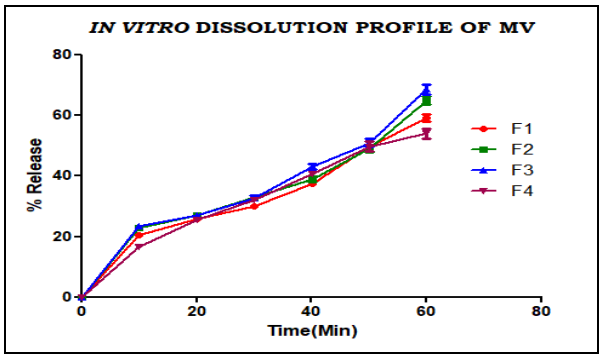


Fig no. 6: Dissolution profile of formulation from F1-F4 for MV

Table no. 12: % cell viability of PTX, combination of MD & MV, Monochoria vaginalis and Momordica dioica on MDA-MB-231 breast cancer cell line.

Concentration (µg/ml)	% cell viability			
	PTX	MD+MV	MV	MD
2	74.074070	69.387760	82.156782	81.251562
4	73.251030	67.041200	80.370370	79.591840
8	71.491230	65.333340	78.039220	77.642270
12	71.354160	63.387980	76.793250	73.777780
16	71.241830	59.195400	74.074070	68.115940
20	68.750000	57.823130	70.621470	64.480870
30	68.253970	52.032520	65.359470	64.102560
40	66.666660	45.528450	59.259260	51.851850

Table no. 13 : % cell viability of PTX, combination of MD & MV, Monochoria vaginalis and Momordica dioica on MDA-MB-231-DR breast cancer cell line.

Concentration (µg/ml)	% cell viability			
	PTX	MD+MV	MV	MD
2	73.25789	70.36548	83.26482	82.36547
4	72.96584	68.32584	80.32145	79.32546
8	71.36480	66.95874	76.32589	75.64589
12	70.33658	63.29542	72.32145	71.23654
16	69.98512	60.34258	68.32542	67.32514
20	69.02654	58.34892	64.58923	63.25478
30	68.32145	51.36480	62.31542	59.62458
40	67.32584	46.32145	58.23564	52.32145

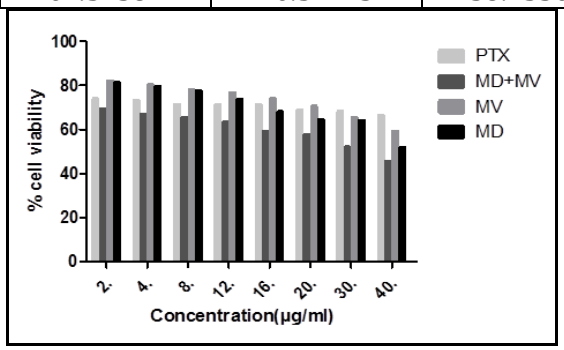


Fig no. 7 : % cell viability of PTX, combination of MD & MV, Monochoria vaginalis and Momordica dioica on MDA-MB-231 breast cancer cell line.

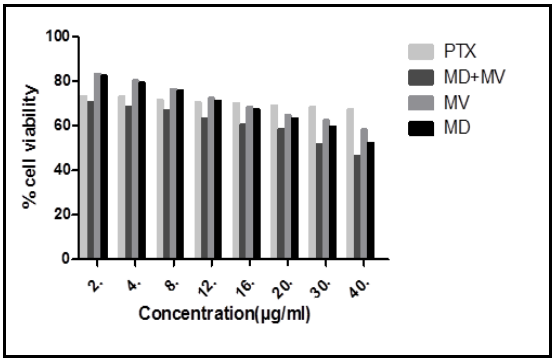


Fig no. 8 : % cell viability of PTX, combination of MD & MV, Monochoria vaginalis and Momordica dioica on MDA-MB-231-DR breast cancer cell line.

Hence it is necessary to carry out moisture uptake studies. 10 tablets from formulation were kept in a desiccator at 37^0C for 24 hrs. Then the tablets were weighed and exposed to 75% relative humidity for 2 weeks. One tablet without drug extract as control was kept to assess the moisture uptake due to other excipients. Tablets were weighed and the percentage increase in weight was recorded.

Drug content: Initially, weighed the tablet and then powdered. The powdered tablet was transferred into a 100ml volumetric flask and adds 6.8 pH Phosphate buffer up to mark. The solution was filtered and the first few ml of filtrate was discarded. 10ml of filtrate was taken into a 50ml of volumetric flask and add 6.8 pH phosphate buffer up to the mark and analysed UV-spectroscopically (JASCO UV Spectrophotometer, Model No. V-630) at 217 and 220nm. The concentration of the content of the drug (µg/ml) was calculated by using the standard calibration curve of the respective drugs.

Disintegration time: It was calculated by using disintegration apparatus (Model: Electrolab-ED-2L). 6 tablets were placed in the tubes along with a plastic disk over the tablets. The disk imparts pressure on the tablets. The tubes were allowed to move up and down in the media as 29-32 cycles per minute in pH 6.8 phosphate buffer media maintained at 37^0C. Time required to pass all tablets through the mesh was determined as its disintegration time.

***In vitro* dispersion time:** Dispersion time of a tablet is determined by placing a tablet in 6 ml of pH 6.8 phosphate buffer and note down the time taken for complete dispersion of tablet.

***In-vitro* drug release:** Dissolution profile of tablet was determined at 37±0.5°C at a stirring rate of 100 rpm using the USP dissolution apparatus II (Model: TAB machines dissolution system (DRS)) in 900 ml of pH 6.8 phosphate buffer. Various aliquot samples were withdrawn with replacement simulated fluid of same amount at 10, 20, 30, 40, 50 and 60 min respectively. Samples were filtered using whatmann filter paper and taken absorbance at wavelength of 217 and 220 nm by UV spectrophotometer.

RESULTS AND DISCUSSION

Preliminary phytochemical screening of ethanolic extracts of Momordica dioica and Monochoria vaginalis

The preliminary phytochemical screening of ethanolic extract of Momordica dioica and Monochoria vaginalis gave the positive reaction for sterol, alkaloids, sugars, flavonoids, amino acid, tannins, triterpenoid and glycosides.

FTIR STUDY

All the prominent and primary peaks were observed in FTIR spectrum. The spectra obtained from the FTIR analysis of plant extracts of Momordica dioica, Monochoria vaginalis, combination of MD + MV and physical mixture are shown in Figure. Plant extracts of Momordica dioica revealed characteristic absorption bands at 3780 cm^{-1} and 3650 cm^{-1} (related to phenolic O-H stretching). Other minor absorption bands observed included the ones at 2349 cm^{-1} (O=C=O stretching), 1760 cm^{-1} (C=O stretching), 1506.41 cm^{-1} (N=O stretching) and 1450 cm^{-1} (C-H stretching). The plant extracts of Monochoria vaginalis spectrum showed strong absorption bands at 3700 cm^{-1} (O-H stretching). Other observed peaks were found at 2349 cm^{-1} (O=C=O) and 1716.65 cm^{-1} (C=O stretching), 1653 cm^{-1} (C=C stretching), 1508.33 cm^{-1} (N-O stretching) and 1456.26 cm^{-1} (C-H stretching). The combination of MD + MV revealed characteristic absorption bands at 3600 cm^{-1} and 3550 cm^{-1} (related to phenolic O-H stretching). Other minor absorption bands observed included the ones at 2349 cm^{-1} (O=C=O stretching), 1775 cm^{-1} (C=O stretching), 1541.12 cm^{-1} (N=O stretching) and 1460 cm^{-1} (C-H stretching). The physical mixture exhibited absorption bands associated with both plant extrcts i.e., at 3853.77 cm^{-1}, 2390 cm^{-1}, 1541.12 cm^{-1}, 1508.33 cm^{-1} and 1330 cm^{-1}. By comparing the peaks of spectrum of plant extracts and excipients, it was observed that no significant changes occurred in peak of Momordica dioica, Monochoria vaginalis, combination of MD + MV and physical mixture. The peaks associated with plant extracts were observed to be slightly shifted, possibly due to weak

intermolecular interactions between the molecules of physical mixture. Hence it was concluded that extracts and excipients was compatible with each other.

THERMAL ANALYSIS

Differential scanning calorimetry (DSC) was used for comparative thermal characterization of the plant extract of Momordica dioica, Monochoria vaginalis, combination of both extracts and physical mixture of both drug extracts with excipients using. The instrument (Model: DSC-60A) was pre-calibrated for heat flow and heat. Differential scanning calorimetry (DSC) was used for comparative thermal characterization of the plant extract of Momordica dioica, Monochoria vaginalis, combination of both extracts and physical mixture of both drug extracts with excipients using. The instrument (Model: DSC-60A) was pre-calibrated for heat flow and heat

Antimitotic Study: Combination of MD & MV showed less mitotic index followed by M. vaginalis, M. dioica, Methotrexate and water. Combination of MD & MV showed highest mitotic inhibition followed by M. vaginalis, M. dioica, Methotrexate and water. This showed potent antimitotic activity of M. dioica and M. vaginalis

Precompressional Studies Of Tablet Blend

The pre-compression study of all batches of blend was evaluated for different derived properties are:-

1) Angle of repose(between 21 to 30),
2) Bulk density (between 0.4050 to 0.4775g/ml)
3) Tapped density (between 0.4120 to 0.4995g/ml)
4) Carr's index (between 10 to 15%)
5) Hausner's ratio (between 1.10 to 1.18)

The results angle of repose and compressibility indicated that the flowability of blend is significantly good. All the results of pre-compression parameters are in the acceptable range.

Post Compressional Study: Tablets were prepared in batches F1 to F4 and evaluated for tablet properties like appearance, weight variation, hardness, thickness, friability, wetting time, water absorption ratio, content uniformity, disintegration time and dissolution.

Physical appearance: The general appearance of tablet was found to be round in shape, brown in color, smooth texture, and odourless. All the tablets passed weight variation test as per the percent weight variation was within the pharmacopoeias limits. Hardness was shown in the range of 3.00 to 4.00 Kg/cm^2 in all the formulations. Friability of all formulations was determined. The friability values of none of the formulations exceeded 1%. The results of friability indicated that the tablets were mechanically stable and can withstand rigor of transportation and handling. Thickness of all tablets was between 3 to 34 mm showing fairly uniform tableting. The results of disintegration of all the tablets were found to be within prescribed limits and satisfied the criteria for the tablet. The value was found to be in the range of 134 to 156 sec. The wetting time was acceptable in the range of 124 to 138 sec. The water absorption ratio was also in the acceptable limit i.e. 140 to 168 sec. The moisture uptake was in the acceptable limit of 2.25 to 4.45%. Dispersion time was found in the range of 88 to 97 sec. The drug content of all batches was found in the range of 91 to 104% and drug release was found to be 59.18±1.27 to 70.35±1.25%.

***IN VITRO* DISSOLUTION STUDIES:** Dissolution study of tablet formulation was carried out in pH 6.8 phosphate buffer over 60 min. The samples were analysed by UV. This study was carried out to check the drug release profile.

OPTIMIZATION: Based on evaluation of post compressional parameters, formulation F3 was considered as an optimized formulation, which shows its potent values complying the results at the optimized level among all batches. The drug content and % drug release of f3 batch for MD & MV was found to be 97.89% & 98.35% and 70.358 ± 1.25%&68.686 ± 1.65 % respectively.

***IN -VITRO* CYTOTOXICITY STUDY:** *In vitro* cytotoxicity study of paclitaxel, combination of Momordica dioica Monochoria vaginalis, Monochoria vaginalis and

Momordica dioica against MDA-MB-231 & MDA-MB-231-DR cell lines was assessed after 72 hrs of incubation by MTT assay. Combination of MD & MV showed less % cell viability followed by paclitaxel, Momordica dioica and Monochoria vaginalis on MDA-MB-231 breast cancer cell line by MTT assay. This showed potent anticancer activity of Momordica dioica and Monochoria vaginalis for the treatment of breast cancer.

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