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Research Article

# SYNTHESIS AND CHARACTERIZATION OF WOUND HEALING ACTIVITY OF (3-(3,5-DICHLORO-2-HYDROXYPHENYL)-1-PHENYL-5-(1-PHENYLPROP-1-EN-2-YL)-1*H*-PYRAZOL-4-YL) (PHENY) METHANONE ON *ALBINO RATS*

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**ABSTRACT**

Synthesis of (3-(3,5-dichloro-2-hydroxyphenyl)-1-phenyl-5-(1-phenylprop-1-en-2-yl)-1*H*-pyrazol-4-yl) (phenyl) methanone (BC3). The compound has been characterized by IR, $H^1$ NMR, Uv, Mass spectroscopy. The compound (3-(3, 5-dichloro-2-hydroxyphenyl)-1-phenyl-5-(1-phenylprop-1-en-2-yl)-1*H*-pyrazol-4-yl)(phenyl) methanone (BC3) was studied on the wounds of *albino rats*. The (BC3) pyrazole produced significant result on tested *albino rats*. The incision wound model (BC3) pyrazole wounds were found to be epithelialise faster and rate of wound contraction was higher, as compare to the control wounds. The results were also comparable to those of standard drug povidone iodine.

**Keywords:** $\Delta^2$ –Pyrazoles, Wound healind activity, IR, NMR and Mass spectra.

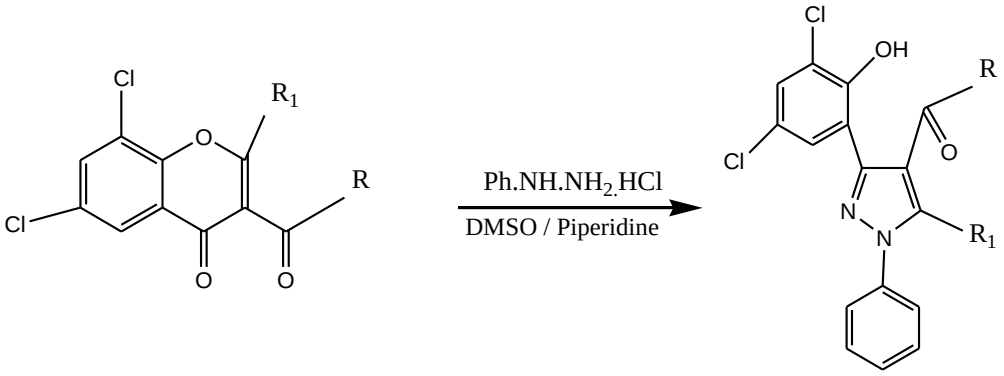
## INTRODUCTION

Pyrazoles is the heterocyclic compounds. Heterocyclic system containing pyrazole ring have attracted the attention of chemists on account of the significant medicinal properties associated with them. It is interesting to know that structure of Pyrazoles found in plant extract. Pyazoles are reported to have properties such as antimicrobial[1], antifungal[2], antibacterial[3], hypoglycamic agent[4], anti-inflammatory[5].However, there was no work found on $\Delta^2$ –Pyrazoles for pharmaceutical study. Hence, the present study was focus towards the effect of (3-(3,5-dichloro-2-hydroxyphenyl)-1-phenyl-5-(1-phenylprop-1-en-2-yl)-1*H*-pyrazol-4-yl)(phenyl)methanone ($\Delta^2$-Pyrazoles) ointment on *albino rats* with special reference to wound healing activity.

## MATERIALS AND METHODS

### Synthesis of (3-(3,5-dichloro-2-hydroxyphenyl)-1-phenyl-5-(1-phenylprop-1-en-2-yl)-1*H*-pyrazol-4-yl) (phenyl) methanone (BC3)

The 3-aroychromone (0.01M) treated with phenyl hydrazine hydrochloride in (20 ml) DMSO with few drops of piperidine under microwave condition for 4 min. The reaction mixture on acidification with HCl (10%), followed by washing with sodium bicarbonate and water gave the compounds. The solid product thus obtained crystallized from ethanol to get the compounds (BC3). The following is the structure of the (BC3) compound.




**Where, R = $C_6H_5$, $C_4H_4O$. $R_1$ = $C_{10}H_{10}O$**

The conformation of structure of (3-(3,5-dichloro-2-hydroxyphenyl)-1-phenyl-5-(1-phenylprop-1-en-2-yl)-1*H*-pyrazol-4-yl) (phenyl) methanone (BC3) compound on the basis of spectral results.

**Spectral data for compound (BC3)**

**(a) FTIR**
(KBr, $cm^{-1}$): (BC3):- 3376 (OH – stretching), 2922 (Ar-CH-stretching), 2853 (C-H stretching in $CH_3$), 1665 (C=O stretching), 1449 (C=N stretching), 758 (C-Cl stretching).

**(b) $H^1$ NMR**
(400MHz, $CDCl_3$, δ ppm): 1.55 (s, 3H,-$CH_3$), 5.59 (s, 1H,-CH), 7.20-8.11 (m, 16H, Ar-H), 12.01(s, 1H, OH).

**(c) UV**
The UV-VIS spectrum of the compound (BC3) recorded in $CHCl_3$ showed λmax value 310 nm corresponding to $n \rightarrow \pi^*$ transition.

**(d) Mass**
(m/z) = 525,510, 433, 405, 303.

**Synthesis of (*Z*)-(3-(3,5-dichloro-2-hydroxyphenyl)-1-phenyl-5-(1-phenylprop-1-en-2-yl)-1*H*-pyrazol-4-yl) (phenyl) methanone (BC3) ointment**

The BC3 compounds ointment was prepared by trituration method. The purpose of this method was ointment base and compound not miscible with each other on melting dosages forms of drugs was prepared as follows:

Firstly the required quantities of compounds (BC3), 0.5 g and 10 g of ointment base were taken (white soft paraffin used as ointment base). Ointment base was first melted. Compound was triturated with the small quantity of ointment base until a homogenous product formed. Remaining quantity of ointment base was added gradually and finally the homogeneous ointment was formed. These ointments freshly prepared daily and apply on the wound area.

**Animals used**

*Albino rats* weighing between 200 - 220 g were used. They were kept in a standard environmental condition and fed with rodent diet and water ad libitum. The animals were allowed to acclimatize for one week before the experiment. The care of laboratory animals was taken according to the guidelines of CPCSEA, Ministry of Forests and Environment, Government of India (registration number 729/02/a/ CPCSEA). The proposed study was carried out after getting permission from the Institutional Animal Ethical Committee, Pusad (CPCSEA/IAEC/CP_PL-15/01-02PD02).

**Wound model**

The *albino rats* weighing 200 - 220 g were divided into four groups. Group one was the control group which received simple oniment base, group two was treated with reference standard (5% w/w povidine iodine) and group three and four received our (BC3) pyrazole compound containing 2.5% w/w ointment topically on wound created on the dorsal back of rats daily till the wounds completely healed excision wound model. Full thickness excision wound was made on the shaved back of the rat by removing a 500sq mm piece of skin and the day on which wound was made considered as the day zero.

**The various groups were treated as follows**

**Group I**

Control [0.5 gm, of simple ointment (vehicle) applied locally].

**Group II**

Standard (5% w/w povidine iodine ointment applied locally).

**Group III**

Low dose, (Low Dose group of rats which were treated with low dose of chlorosubstituted pyrazole (BC3) ointment once a day for 20 days.

**Group IV**

Group IV was the high dose group of rats were immediately after cutting, cutting areas were covered with high dose chlorosubstituted pyrazole (BC3) ointment once a day for 24 days.

Animals divided into four groups were treated as described above. The percentage of wound closure was recorded on days 0, 8, 16, and 24. In this period wound area was traced and measured. The actual value was converted into percent value taking the size of the wound at the time of wounding as 100%.

**RESULT AND DISCUSSION**

The rates of contraction of group I to group III of experimental wounds are represented in Table 1, 2 and graph 4.1. The treated wounds were found to contract much faster as compared to control wound. At the end of 24$^{th}$ day after cut wound creation, the control group rats showed 63.20 % of wound contraction indicating the natural healing property of skin. The standard drug povidine iodine treated rat shows 97% of wound contraction. The group III of low dose of pyrazole (BC3) ointment shows 97.17% wound contraction and high dose of pyrazole (BC3) ointment shows 97.69% indicating faster wound healing because the presence of cinnamyl substituted pyrazole (BC3) moiety.

**Table1: Effect of topical application of 2.5 % w/w ointment of (BC3) pyrazole compound on incision wound model**

| Group Names | 0 th day | 8th day | 16th day | 20th day | Epithelization time in (dms) |
|---|---|---|---|---|---|
| Control | 502.61 | 415.82 | 280.20 | 182.23 | 25 |
| | 504.32 | 408.92 | 276.02 | 174.42 | 24 |
| | 497.20 | 420.10 | 288.03 | 186.80 | 25 |
| Standard | 504.52 | 296.31 | 180.46 | 12.04 | 18 |
| | 496.03 | 288.19 | 188.52 | 10.28 | 17 |
| | 508.2 | 300.20 | 176.72 | 14.12 | 16 |
| Low dose | 500.12 | 356.71 | 240.52 | 13.58 | 22 |
| | 504.54 | 362.23 | 245.68 | 14.20 | 21 |
| | 502.01 | 352.41 | 252.71 | 14.80 | 20 |
| High dose | 503.3 | 325.62 | 194.33 | 12 | 18 |
| | 509.2 | 320.81 | 188.20 | 11.20 | 19 |
| | 499.2 | 329.42 | 198.72 | 11.42 | 17 |

**Table 2: Percentagewise effect of treatments on wound contraction photographs of wound healing activity**

| Treatments | 0$^{th}$ day | 8$^{th}$ day | 16$^{th}$ day | 24$^{th}$ day | Epithilizati-on time in days |
|---|---|---|---|---|---|
| Group I (Control) | 0% ± 2.78 | 17.22 % ± 1.60 | 43.87% ± 1.98 | 63.20% ± 1.34 | 24 ± 0.44 |
| Group II (Povidine iodine) | 0% ± 2.81 | 40% ± 1.31 | 63% ± 1.40 | 97% ± 1.02 | 17 ± 0.66 |
| Group III Low dose of pyrazole (BC3) ointment | 0% ± 0.87 | 28% ± 2.00 | 50% ± 1.41 | 97.17% ± 0.41 | 21 ± 0.66 |
| Group III High dose of pyrazole (BC3) ointment | 0% ± 1.2 | 35% ± 2.22 | 60.78% ± 1.53 | 97.69% ± 0.30 | 18 ± 0.66 |

**Group I: Control Group of rats treated with simple ointment base**

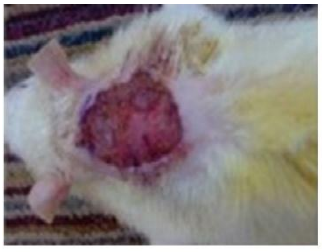


**Fig. 1: Treatment for 0 day**

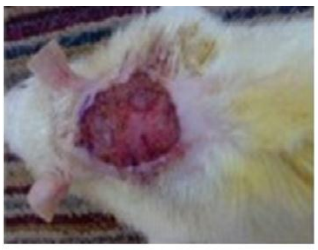


**Fig. 2: Treatment for 8 days**

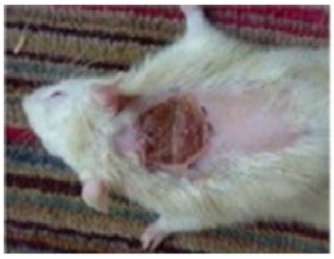


Fig. 3: Treatment for 16 days

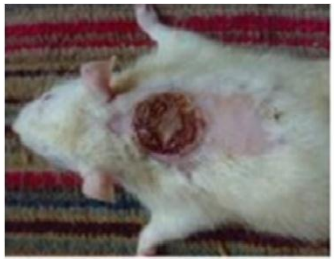


Fig. 4: Treatment for 24 days

**Group II: Standard drug (5% w/w povidine iodine)**

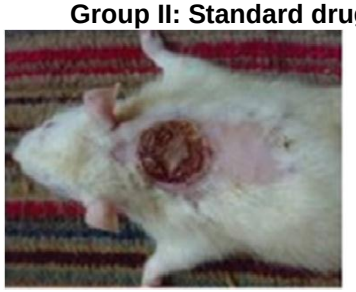


Fig. 5: Treatment for 0 day

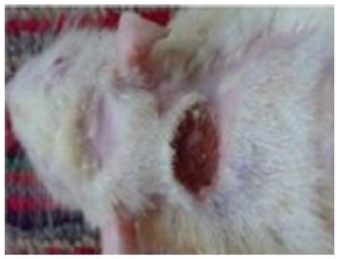


Fig. 6: Treatment for 8 days

Fig. 4.8: Treatment for 16 day

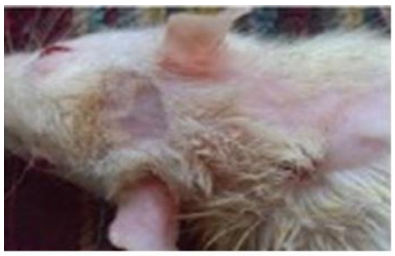


Fig. 4.9: Treatment for 24 days

**Group III: Low dose of pyrazole (BC3) ointment**

Fig. 4.10: Treatment for 0 day

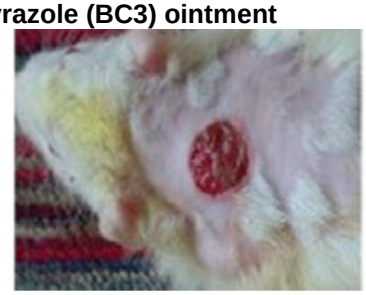


Fig. 4.11: Treatment for 8 days

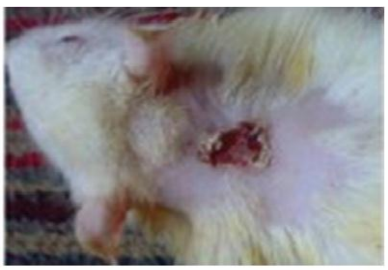


Fig. 4.12: Treatment for 16 day

Fig. 4.13: Treatment for 24 days

**Group IV: High dose of pyrazole (BC3) ointment**

**Fig. 4.14: Treatment for 0 day**

**Fig. 4.15: Treatment for 8 days**

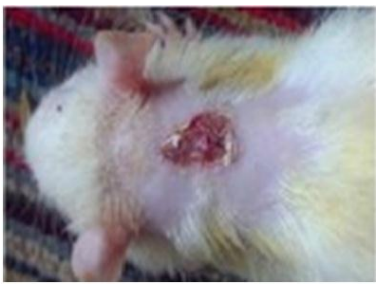


**Fig. 4.16: Treatment for 16 days**

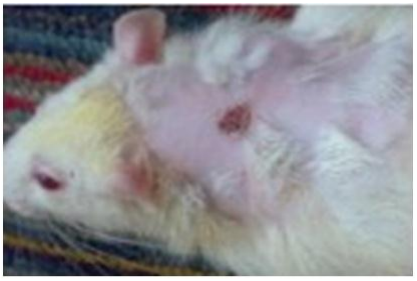
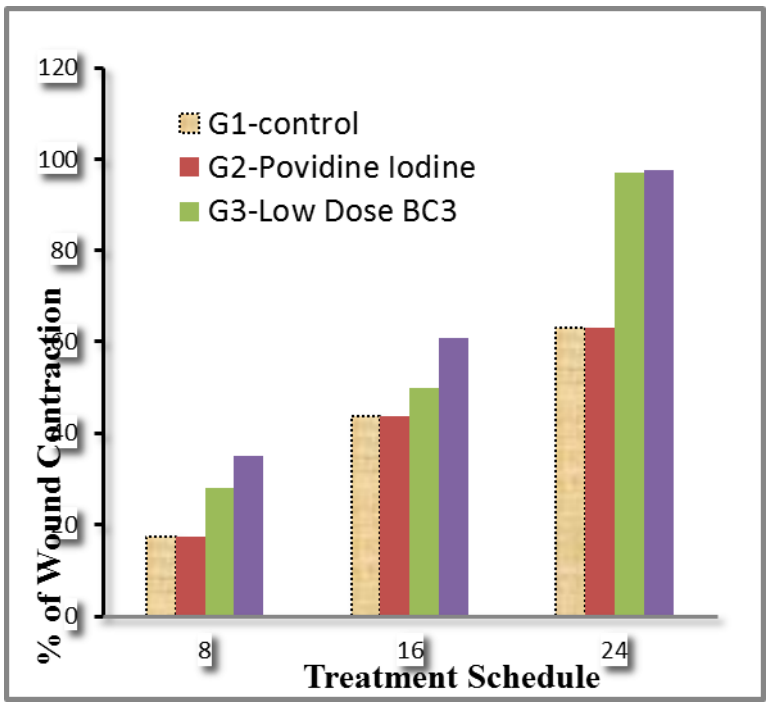


**Fig. 4.17: Treatment for 24 days**




**Graph. 1: Variation of wound contraction % with treatment schedule**

## CONCLUSION

From the results it was concluded that the wound healing activity of the compound 3-(3,5-dichloro-2-hydroxyphenyl)-1-phenyl-5-(1-phenylprop-1-en-2-yl)-1*H*-pyrazol-4-yl) (phenyl) methanone (BC3) high dose was found closer (wound contraction 97.69% on day 24$^{th}$day and epithelization time on day 18) to that of standard drug povidine iodine (97%) wound contraction on 24$^{th}$day and epithelization period on day 17), due to the presence of *p*-methoxy phenyl ring (electron donating group) in compound might have been favoured an significant wound healing activity. It is observed that the p-value for rows among the four groups is 0.000317* and calculated thought the days is 0.002479** both the values of * and ** is less than 0.05 ($p < 0.05$). All the results have proved that the treatment of chlorosubstituted pyrazole (BC3) compound has increased healing potential of cut wounds in *albino rats* under investigation.

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