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JOURNAL CLUB ACTIVITY

Department of Pharmaceutics

Attendance cum response sheet for Journal Club of Department of Pharmaceutics

Date & Time: 08/02/2021; 02.00 pm

Name of the Facilitator: Mr. Nilesh Bhosale

Title of the paper discussed: Pharmaceutical Cocrystal of Piroxicam: Design, Formulation and Evaluation

Sr. No.	Name of the member	Signature	Evaluation of today's meeting/suggestions
1.	Mr. J. V. Shinde	Shinde ..	The detailed study on SEM is expected in these types of activities.
2.	Mr. N. R. Bhosale	Bhosale ..	Comparitive study with conventional tablet is required.

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Research Article

Pharmaceutical Cocrystal of Piroxicam: Design, Formulation and Evaluation

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Abstract

Purpose: Cocrystallisation of drug with coformers is a promising approach to alter the solid sate properties of drug substances like solubility and dissolution. The objective of the present work was to prepare, formulate and evaluate the piroxicam cocrystal by screening various coformers.

Methods: Cocrystals of piroxicam were prepared by dry grinding method. The melting point and solubility of crystalline phase was determined. The potential cocrystal was characterized by DSC, IR, XRPD. Other pharmaceutical properties like solubility and dissolution rate were also evaluated. Orodispersible tablets of piroxicam cocrystal were formulated, optimized and evaluated using 3^2 factorial design.

Results: Cocrystals of piroxicam-sodium acetate revealed the variation in melting points and solubility. The cocrystals were obtained in 1:1 ratio with sodium acetate. The analysis of Infrared explicitly indicated the shifting of characteristic bands of piroxicam. The X-Ray Powder Diffraction pattern denoted the crystallinity of cocrystals and noteworthy difference in 2θ value of intense peaks. Differential scanning calorimetry spectra of cocrystals indicated altered endotherms corresponding to melting point. The pH solubility profile of piroxicam showed sigmoidal curve, which authenticated the pKa-dependent solubility. Piroxicam cocrystals also exhibited a similar pH-solubility profile. The cocrystals exhibited faster dissolution rate owing to cocrystallization as evident from 30% increase in the extent of dissolution. The orodispersible tablets of piroxicam cocrystals were successfully prepared by direct compression method using crosscarmelose sodium as superdisintegrant with improved disintegration time (30 sec) and dissolution rate.

Conclusion: The piroxicam cocrystal with modified properties was prepared with sodium acetate and formulated as orodispersible tablets having faster disintegration and greater dissolution rate.

Introduction

The solubility and dissolution rate of drugs is a decisive factor after oral administration for rate and extent of absorption. This factor offers key challenge for the development and formulation of effective drug in the pharmaceutical industry. More than 60% drugs coming from synthesis and 40% drugs in the development are poorly soluble and face bioavailability problems. Various strategies have been well documented to enhance solubility and dissolution of poorly soluble drugs *viz* salt formation, solid dispersion, microemulsification, cosolvency, inclusion complex formation with cyclodextrin etc.[1-4]

Pharmaceutical cocrystal is a budding tool to modify solubility, dissolution rate and physical and chemical stability of drug substances while keeping the pharmacological effect of drug unchanged. Cocrystal can be defined as stoichiometric multi-component system connected by non-covalent interactions in which two distinct components are solid under ambient conditions. A pharmaceutical cocrystal constitutes active pharmaceutical ingredient and benign substance called a coformer. The cocrystals of piroxicam were reported with different carboxylic acid by solution crystallization, melt crystallization and solvent drop grinding method.[5-7]

Piroxicam is nonsteroidal anti-inflammatory BCS class II drug with prevalent solubility problem. It takes about 3-5 hrs to reach peak plasma concentration after oral administration. This indicates poor absorption of piroxicam after oral administration. Drug dissolution in biological fluid is slow due to limited aqueous solubility leading to erratic bioavailability and suboptimal efficacy. Drug dissolution *in vivo* is the rate-controlling step in drug absorption. It is indicated for acute or long-term use in the relief of signs and symptoms of osteoarthritis and rheumatoid arthritis.[8-12]

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Rapid onset and improved bioavailability are desirable for analgesics. Hence there is strong scientific and clinical need to prepare novel forms of piroxicam possessing modified solubility and dissolution rate which can be formulated for oral administration. Accordingly aim of the present study was to prepare pharmaceutical cocrystal of piroxicam, formulation of orodispersible tablets containing piroxicam cocrystal and its evaluation.[13-20]

Materials and Methods

Piroxicam was gift sample from the Shreya Life sciences Aurangabad (India). All other chemicals were purchased from the SD Fine Chemicals Mumbai (India). Double distilled water was used throughout the research.

Preparation of cocrystal

Dry grinding method was employed for the preparation of piroxicam cocrystals. Drug and coformer were mixed in different molar ratio (1:1 and 1:2) in mortar and pestle for 45 min to form cocrystals. This was dried an overnight at ambient temperature and stored in tight containers. The 20 coformers screened were adipic acid , benzoic acid, cinnamic acid, citric acid, glutaric acid, p-hydroxybenzoic acid, hippuric acid, malonic acid,resorcinol, saccharine sodium, 1-hydroxy-2-napthoic acid, sodium acetate, urea, catechol, ferulic acid, aerosil-200, nicotinamide, para amino benzoic acid, anthranilic acid and succinic acid.[21,22]

Determination of melting point

Melting point of the compounds were estimated using digital melting point apparatus.

Saturation solubility

The solubility was determined by dissolving excess quantity of pure drug and cocrystals in the 10 ml vials containing water. The vials were subjected to agitation on rotary shaker and allowed to stand for equilibrations for 24 hrs. The samples were filtered after 24 hrs, diluted with distilled water and analyzed by UV Spectrophotometer at 353 nm.[23]

IR spectroscopy

IR spectroscopy was employed to determine the probable interaction between drug and coformer. The samples were dispersed in KBr pellet and scanned using Shimadzu IR Spectrophotometer between 4000-400 cm^{-1} with resolution of 4 cm^{-1}.

Differential scanning calorimetry

The thermal behavior of drug alone and cocrystal was determined by Differential scanning calorimetry (DSC) studies by Mettler Toledo DSC 822e Module. Weighed samples were heated in aluminum pans at a rate of 5 °C/min, from 0 to 300 °C temperature range, under a nitrogen stream. The instrument was calibrated using indium and empty aluminum pan was used as a reference.

Powder X-ray diffraction

The silicon sample holders were utilized to get diffraction patterns of pure Piroxicam and cocrystal (Bruker D8 Advance Diffractometer). The instrument was equipped with a fine focus X-ray tube and each sample was placed on to a goniometer head that was motorized to permit spinning of the sample during data acquisition.

Effect of pH on solubility of piroxicam

The solubility of piroxicam was determined in the various buffers, pH 1 to pH 10 individually. Excess amount of piroxicam was added in the vials containing 10 ml of each buffer. The vials were subjected to rotary shaking and allowed to stand for equilibrations for 24 hrs. The samples were filtered after 24 hrs, diluted with distilled water and analyzed by UV Spectrophotometer at 353 nm.[24]

Effect of pH on solubility of piroxicam cocrystal

The piroxicam cocrystals in excess quantity were dissolved in hydrochloric acid buffer (pH 1.2), acetate buffer (pH 4.5) Phosphate buffer (pH 6.8 and pH 7.4). The vials were subjected to agitation on rotary shaker and allowed to stand for equilibrations for 24 hrs. The samples were filtered after 24 hrs, diluted with distilled water and analysed by UV Spectrophotometer at 353 nm.[25]

Powder dissolution study

Dissolution studies were performed in 0.1 N HCl (900 ml) for 60 min at 37±0.5°C and 50 rpm using USP type II dissolution test apparatus (Electrolab, Mumbai, India). The pure drug and cocrystal equivalent to 20 mg of drug was used for the study. The 5 ml of samples were withdrawn after specified time interval and analyzed by UV spectrophotometer at 353 nm.

Formulation of orodispersible tablets of piroxicam cocrystal by 3^2 full factorial design

An accurately weighed quantity of piroxicam cocrystal equivalent to drug dose and all other ingredients were passed through 60-mesh sieve and mixed in vertical blender for 30 min. The resulting blend was directly compressed into tablets. The quantity of all components was constant except superdisintegrant and binder. Round concave tablets of 200 mg in weight and 4 mm in diameter were prepared using Cadmach multi station tablet compression machine. Table 1 outlines the composition of various orodispersible tablet formulations.

Evaluation of pre-compression parameters

Prior to compression, powder blends were evaluated for tapped density, bulk density, and flow and compressibility parameters. Flow properties of powder were determined by angle of repose and compressibility by Carr's index and Hausner ratio.

Table 1. Composition of factorial design formulations

Ingredients	F1	F2	F3	F4	F5	F6	F7	F8	F9
Piroxicam cocrystal	24.96	24.96	24.96	24.96	24.96	24.96	24.96	24.96	24.96
Crosscarmillose sodium	10	7	10	4	7	4	10	7	4
MCC PH102	103.04	100.04	100.04	109.04	106.04	106.04	97.04	110.04	103.04
Mannitol	54	54	54	54	54	54	54	54	54
PVP K-30	4	10	7	4	4	7	10	7	10
Aspartame	2	2	2	2	2	2	2	2	2
Magnesium Stereate	2	2	2	2	2	2	2	2	2
Total	200	200	200	200	200	200	200	200	200

Evaluation of post compression parameters

Thickness and weight variation

The thickness of the tablets was measured using a digital Vernier caliper. Five tablets were randomly taken from each formulation and thickness of each of these tablets was measured. The results are expressed mean±standard deviation (SD). Twenty tablets were selected at random and average weight was determined using an electronic balance (Shimadzu). Tablets were weighed individually and compared with average weight.

Hardness and friability

Five tablets were randomly selected from each batch and hardness of tablets was determined by using Monsanto hardness tester. The mean values and standard deviation for each batch were calculated. The friability of tablets was measured using USP type Roche friabilator. Preweighed tablets (equivalent to 6.5 g) were placed in plastic chambered friabilator attached to motor revolving at a speed of 25 rpm for 4 min. The tablets were then dedusted, reweighed, and percent weight loss was calculated using the formula, % friability = ((initial weight–final weight)/ initial weight)×100.

Wetting time

Six circular tissue papers of 10 cm diameter were placed in a Petri dish and 10 ml of water containing amaranth dye was added to it to identify complete wetting of tablet surface. A tablet was carefully placed on the surface of tissue paper in Petri dish at ambient temperature. The time taken by water to reach upper surface of the tablet and to completely wet the tablet was noted as wetting time. The study was performed in triplicate and time was recorded using stopwatch.

In vitro disintegration time

The digital tablet disintegration test apparatus (Veego) was used to determine *in vitro* disintegration time (DT) using distilled water at 37±2°. The time in seconds taken by tablet for complete disintegration with no residue remaining in apparatus was recorded as mean±SD.

In vitro drug release study

The drug release studies were performed using the USP dissolution test apparatus (VDA-6DR USP Stds.,Veego) employing paddle method. The dissolution test was performed using 900 ml of 0.1 N hydrochloric acid at 37±0.5° and paddle speed of 50 rpm. Samples (5 ml) were collected at predetermined time intervals (5 min) and replaced with equal volume of fresh medium. The study was continued for 60 min, samples were then filtered through 0.45 µm membrane filter and analyzed at 353 nm using UV spectrophotometer (Shimadzu).

Water Absorption Ratio

A piece of tissue paper folded twice was placed in small Petri dish (7.5cm) containing 7 ml water. A tablet was put on the tissue paper and allowed to wet completely. The wetted tablet was then weighed. The water absorption ratio R was determined using following equation $R=W_a-W_b/W_a\times100$

Drug content

Twenty tablets were weighed and powdered. Powder equivalent to a single dose of piroxicam was weighed, dissolved in few ml of methanol, diluted with 0.1N hydrochloric acid and assayed for drug content at 353 nm using UV-Visible spectrophotometer (Shimadzu).

Stability study

The optimized formulation was subjected to stability study according to ICH guidelines, at room temperature, 30±2°/60%RH±5% and 40±2°/75% RH±5% condition in stability chamber (HMG, India) for three months. Tablets were assayed for drug content for 90 days at the interval of one month.[26,27]

Preliminary trial formulations of piroxicam cocrystal were framed by direct compression method using varying concentration of superdisintegrant (crosscarmellose sodium) and binder (PVP K-30). The 3^2 factorial design was used for the optimization of variables (Design Expert 8.0.7.1). The two independent factors, concentration of crosscarmelose sodium (X1) and concentration of PVP K-30 (X2), were set to three different levels and experimental trials were performed for all nine possible combinations. The dependent responses measured were *in vitro* disintegration time (Y1) and percent drug release (Y2).

Results and Discussion

The 20 coformers were screened for potential cocrystal formation with piroxicam by dry grinding method. Only sodium acetate successfully interacted with piroxicam, giving novel cocrystal form. The obtained piroxicam cocrystal was subjected to physichochemical evaluation and orodispersible tablet formulation.

Melting point and saturation solubility

The melting points of pure drug, coformers and cocrystals were determined and recorded in Table 2. The saturation solubility of pure drug and potential cocrystals were also determined and reported in Table 2. Both these parameters were estimated as a preliminary screen for potential cocrystals. Melting points of cocrystals were lesser than the piroxicam. The depression of melting points revealed multi component system and designated formation of cocrystals. The modified melting points of cocrystals might be attributed to the interaction between piroxicam and coformers, change in crystallinity of molecules or different packing arrangement. This interaction results in some change in molecular arrangement leading to new crystal form possessing modified physical properties *viz.* melting point and/or solubility.[28]

Solubility of cocrystals was increased with each coformer but remarkably improved (5 folds) with sodium acetate. This indicates the successful interaction of piroxicam with coformers and formation of cocrystals. The interaction between the pyridine and amide nitrogen atom of piroxicam and sodium acetate might have formed the cocrystal. The hydrogen bonding between pyridine and amide nitrogen of piroxicam and carboxylic acid leading to cocrystal formation was reported.[29] Similar studies pertaining to solubility enhancement were reported with cocrystals of fluoxetine hydrochloride, niclosamide, meloxicam etc.[30-32] Based on the results, piroxicam-sodium acetate cocrystal (called as piroxicam cocrystal in the following sections) was further characterized and used for the formulation of orodispersible tablets.

Table 2. Melting point and solubility of cocrystals

Drug/Coformer	Melting point coformer	Cocrystal melting point (1:1)	Solubility* (mg/ml) (1:1)	Cocrystal melting point (1:2)	Solubility* (mg/ml) (1:2)
Piroxicam	198-200		0.09769±0.32		
Piroxicam-sodium acetate	324	184-187	0.49166±0.61	189-191	0.30912±0.88
Piroxicam-saccharine sodium	277	181-183	0.11447±0.60	178-179	0.21515±0.49
Piroxicam-Urea	132-135	171-173	0.10727±0.65	175-177	0.13141±0.56
Piroxicam-Nicotinamide	125-131	162-165	0.10470±0.95	158-160	0.13532±0.77
Piroxicam-resorcinol	109 -112	185-187	0.10155±1.6	189-190	0.19292±0.23

*Average of three determinations Mean±SD

Computational study

The probable interaction between piroxicam and sodium acetate was studied by Schrödinger (Jaguar) software. The gas free energy of the piroxicam, sodium acetate and cocrystal was calculated. The piroxicam-sodium acetate complex showed least free energy (-1671.29) as compared to piroxicam (-1442.71) and sodium acetate (-228.49). The complex indicated greater stability owing to least free energy. Hence piroxicam may interact with sodium acetate via hydrogen bonding.

IR spectroscopy

The IR spectrum for pure drug, coformer and cocrystal was recorded and shown in Figure 1. The principle bands were identified and associated changes were recorded. The IR spectrum of pure piroxicam shows the presence of the characteristic peaks which were recorded at 3334 cm^{-1} for NH stretching, SO2 stretching at 1147 cm^{-1}, C-S stretching at 687 cm^{-1}. The IR spectrum of sodium acetate revealed an absorption band at 3400 cm^{-1} which can be assigned to O-H stretching. In addition C=H and C-O-C stretching bands were recorded at 1691 cm^{-1} and 1012 cm^{-1} respectively. These spectra are in good agreement with the published data.[33] The IR bands were significantly changed in the cocrystal in comparison to pure drug and coformer indicating interaction between drug and coformer. These alterations were manifested in the peaks corresponding to NH stretching which was observed at 3351 cm^{-1}. This indicates cocrystal formation as peak shifted slightly, and became broader in the cocrystal. Many new peaks were observed in the cocrystal spectra supporting the formation of cocrystal. Similar changes in the IR spectrum of other drug like hydrochlorothiazide were reported and taken as indication of the cocrystal formation. Hence the changes recorded in the study can be taken as a signal of the cocrystal formation between the drug and coformers.[34]

Differential scanning calorimetry

Piroxicam, sodium acetate and piroxicam-sodium acetate cocrystal were characterized by DSC. The pure drug and coformer showed characteristic endothermic peak at 200.39 °C and 323.58 °C respectively corresponding to their melting point. Similar thermal behavior was reported for the drug.[35] The cocrystal showed substantial difference in the melting point (188.16°C) in comparison to pure drug (200.39°C) and coformer (323.58°C).

Moreover, the peak onset for pure drug was obtained at 199.60 °C whereas 182.57 °C for cocrystal which indicates possibility of formation of the cocrystal. The peak corresponding to coformer fusion was not detected in the DSC of cocrystal that confirms the formation of cocrystal and thus absence of physical mixture. The change in the thermal properties were reported as evidence for the formation of cocrystal. Hence the present investigation denotes the formation of cocrystal.[36] The DSC spectrum is shown in Figure 2.

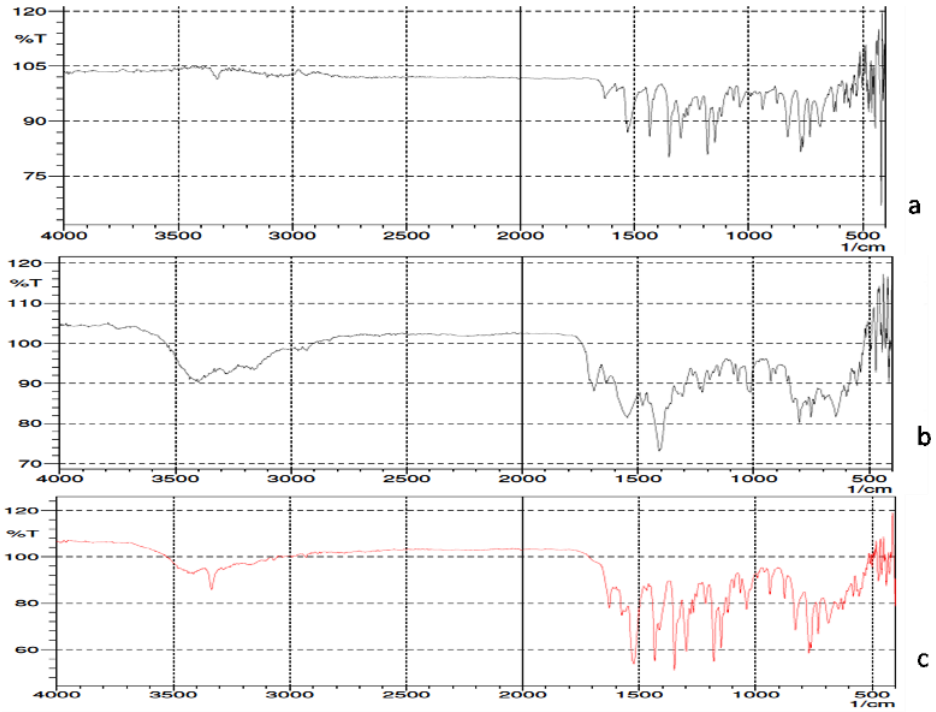

Figure 1. FTIR Spectra of a) Piroxciam b) Sodium acetate c) Piroxicam cocrystal

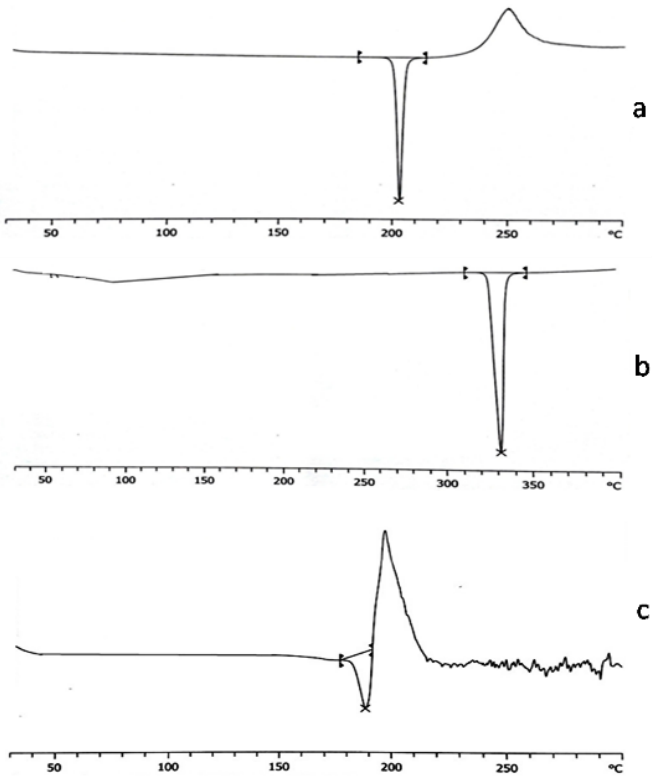

Figure 2. DSC thermogram of a) Piroxciam b) Sodium acetate c) Piroxicam cocrystal

Powder X-ray diffraction

The PXRD patterns for piroxicam, sodium actetate and cocrystal are shown in Figure 3. The materials in the powder state give distinctive peaks of varying intensities at certain positions. The diffractogram of the piroxicam showed characteristic diffraction peaks at different 2θ values (17.6, 17.7, 21.7, 27.4, 27.5, 27.8) indicating the crystalline nature. In addition diffraction peaks obtained for sodium acetate were 17.8, 26.7, 26.8, 35.9, 36, 36.1 2θ values. Similar diffraction pattern was reported in the previous investigations. The PXRD pattern of the cocrystal was distinguishable from its components and some additional diffraction peaks were appeared which did not exist in the pure drug or coformer. The additional diffraction peaks for cocrystal were obtained at 2θ values of 12.4, 12.5, 14.4, 14.5, 17.5, 17.6, 17.7, 17.8, 22.4, 22.5 27.3, 27.4, 27.5, 29.7, and 36.6. The appearance of new diffraction peaks in the diffractogram of cocrystal shows formation of new crystalline phase (cocrystal). The formation of cocrystals based on the PXRD pattern had been well documented, which showed new peaks that differ from the peaks corresponding to its input components.[37]

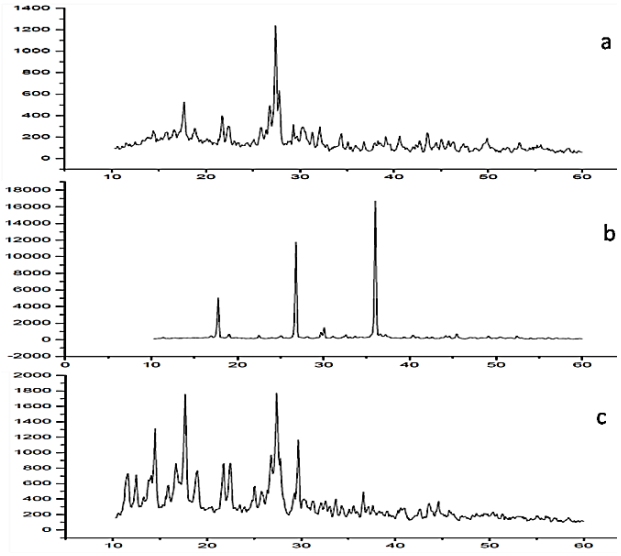

Figure 3. PXRD pattern of a) Piroxciam b) Sodium acetate c) Piroxicam cocrystal

Effect of pH on solubility of piroxicam

The solubility of piroxicam was determined in the variety of buffers having pH 1to 10. The pH solubility profile was reported in Figure 4. The solubility of proxicam was different in the various buffers. The sigmoidal solubility curve was obtained. The solubility of piroxicam was not changed substantially till pH 5 but thereafter increased rapidly. The piroxicam is weakly acidic (pK_{a1} 1.86 and pK_{a2} 5.46) showing pH dependant ionization and solubility.

Effect of pH on solubility of piroxicam cocrystal

The solubility of piroxicam cocrystal was estimated in the buffer solutions having pH 1.2, 4.5, 6.8 and 7.4. The pH solubility data was presented in the Figure 4. Cocrystal showed pKa dependant solubility and capricious behavior at different pH. The solubility of cocrystal was much greater at pH 7.4 as compared to piroxicam. This advocated the pairing of piroxicam cocrystals even at higher pH.[38]

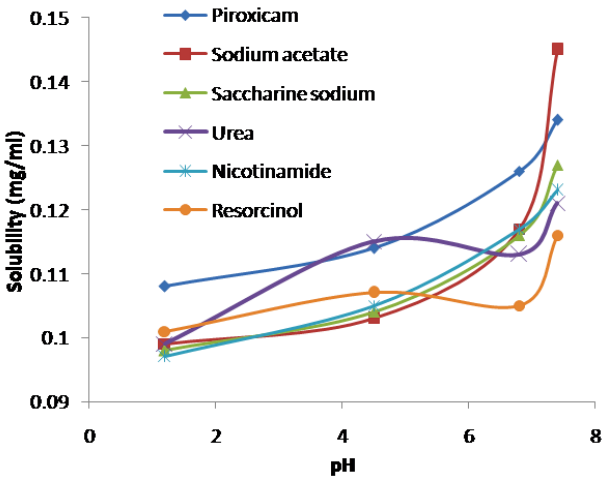

Figure 4. pH solubility profile of piroxicam and piroxicam cocrystal

Powder dissolution study

The dissolution rate plays crucial role in the bioavailability of drugs with poor solubility. The dissolution experiment was conducted on the pure drug and cocrystal. The dissolution profile of the pure drug and the prepared cocrystal are shown in Figure 5. The dissolution profile of pure drug indicates slow dissolution rate with only 15.62% of the drug being dissolved in the first 10 min. The total amount of drug dissolved in 60 min was 49.81% and calculated dissolution efficiency was only 29.8%. However cocrystal of the piroxicam resulted in significant increase in the dissolution rate. The amount of drug dissolved in first 10 min was 64.80% and the total amount dissolved was 99.10% with dissolution efficiency of 85.30%. This can indicate the weaker crystalline structure of the formed cocrystal as evident from higher dissolution rate. Moreover greater dissolution of piroxicam from cocrystal can be attributed to changed crystallinity pattern, size and shape and crystal habit of cocrystal that lead to enhanced solubility of cocrystal in the dissolution media. Cocrystallization had been well documented as a competent technique for dissolution enhancement.[39] The similarity factor test denotes the dissolution of pure drug was dissimilar to the prepared cocrystal (F2 value 20%).

Formulation of orodispersible tablets of piroxicam cocrystal by 3^2 full factorial design

The present study was focused on formulation of orodispersible tablet of prepared piroxicam cocrystal. Preliminary studies were performed to optimize the concentration of superdisintegrant (crosscarmellose sodium) and binder (PVP K-30). The developed factorial formulations were subjected to evaluation of various precompression parameters and the results are depicted

in Table 3. All the formulations exhibited good flow properties. The result of post compression parameters showed that, all the formulated tablets were of uniform weight with acceptable weight variation and thickness. Hardness of all formulations was maintained at 3.2-3.6 kg/cm^2 and friability loss was between 0.72 to 0.86%. The hardness and friability studies revealed that the tablets possessed good mechanical resistance. The orodispersible tablets showed drug content between 98.04-99.48% which was within acceptable limits. The F1 batch was promising as it exhibited least disintegration time (29± 0.12 sec) and wetting time (21±0.58 sec), and maximum water absorption ratio (97.65±0.25%) (Table 3). The disintegration time was decreased with increasing concentration of superdisntegrant owing to sufficient swelling of tablet required for disintegration and wicking action of superdisintegrant.[40]

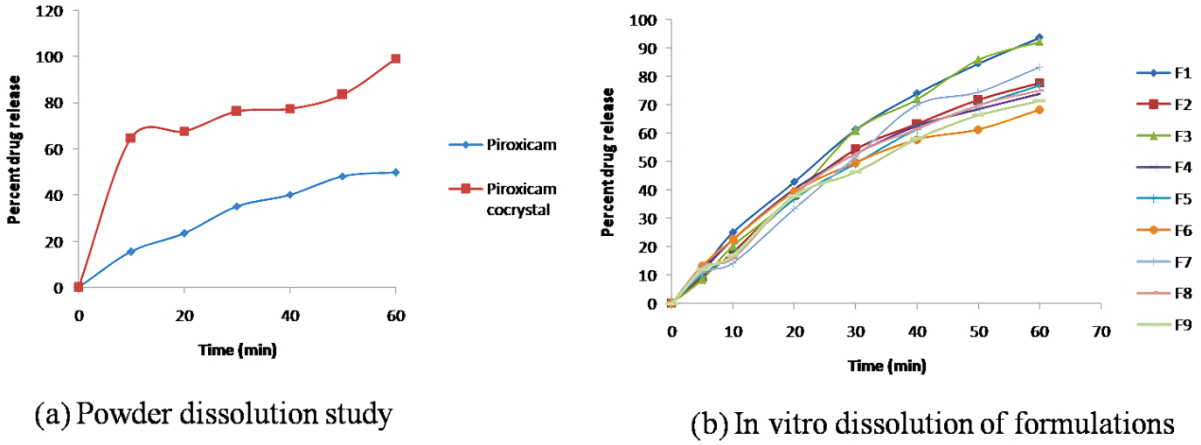

Figure 5. *In vitro* dissolution study

Table 3. Pre-compression and post compression parameters of designed formulations

Precompression parameters									
Parameters	**F1**	**F2**	**F3**	**F4**	**F5**	**F6**	**F7**	**F8**	**F9**
Bulk density (gm/cm^3)	0.331±0.026	0.335±0.014	0.331±0.012	0.334±0.015	0.336±0.095	0.331±0.065	0.334±0.065	0.332±0.036	0.334±0.039
Tapped density (gm/cm^3)	0.392±0.016	0.401±0.069	0.409±0.095	0.409±0.095	0.419±0.065	0.406±0.068	0.411±0.065	0.409±0.098	0.410±0.079
Hausner's ratio	1.18±0.058	1.19±0.065	1.23±0.085	1.22±0.098	1.24±0.069	1.22±0.095	1.23±0.061	1.23±0.091	1.22±0.013
Compressibility index (%)	15.56±0.068	18.45±0.098	19.07±0.065	18.33±0.065	19.80±0.073	18.47±0.034	18.73±0.016	18.82±0.064	18.53±0.043
Angle of repose (θ)	29.92±0.032	26.96±0.065	29.54±0.021	30.92±0.064	30.96±0.015	31.31±0.024	28.25±0.054	29.51±0.064	31.27±0.079
Post compression parameters									
Weight Variation (mg)	200±1.3	201±1.9	200±1.5	201±0.9	201±1.3	199±1.3	198±1.1	202±2.6	200±1.6
Hardness (kg/cm^2)	3.2±0.96	3.4±0.98	3.5±0.62	3.5±0.12	3.2±0.98	3.5±0.65	3.6±0.95	3.5±0.06	3.4±0.56
Thickness(mm)	4.22±0.7	4.18±0.8	4.15±0.4	4.16±0.8	4.22±0.2	4.17±0.2	4.14±0.1	4.16±0.5	4.19±0.3
Friability (%)	0.85±0.7	0.80±0.5	0.76±0.9	0.78±0.5	0.86±0.2	0.79±0.5	0.72±0.8	0.76±0.8	0.81±0.0
Disintegration time (sec)	29±0.12	41±0.95	32±0.65	36±0.97	33±0.58	32±0.65	42±0.15	34±0.85	40±0.25
Wetting time(sec)	21±0.58	30±0.35	22±0.36	26±0.86	23±0.58	29±0.35	32±0.76	29±0.68	24±0.25
Water absorption ratio(%)	97.65±0.25	81.35±0.98	88.59±0.5	84.62±0.36	89.74±0.49	88.16±0.36	79.39±0.84	89.06±0.62	83.39±0.67
Drug content (%)	99.48±0.2	98.04±0.5	99.18±0.8	99.08±0.9	99.01±0.4	99.02±0.5	99.44±0.5	98.46±0.7	98.48±0.3

Results are expressed as mean±standard deviation (n=3)

In vitro drug release study

The study was aimed to evaluate the *in vitro* dissolution behavior of developed formulations. The drug release at 60 min was considered and depicted in Figure 5. The F1 batch showed maximum drug release (93.69±0.12%) although F3 batch exhibited comparable drug release. This might be due to lower concentration of binder and greater concentration of superdisintegrant. Depending on the entire evaluation parameters, F1 batch was selected as optimized formulation and subjected for stability study.[41]

ANOVA study

Analysis of variance for dependent variables, disintegration time and percent drug release was performed. The coefficients X1(Crosscarmellose

sodium) and X2 (PVP K-30) showed significant effect ($p<0.05$) on the selected responses.

Response surface plots

The response surface plots were generated for disintegration time and percent drug release and effect of independent variables, X1 and X2 was studied on the responses Figure 6.

The effect of formulation variables on disintegration time can be described by the model equation

Disintegration Time (sec) = +27.666-0.277 * X1 + 1.3868 * X2

The negative sign for coefficient X1 indicates increase in concentration of crosscarmellose sodium decreased the disintegration time and positive sign for X2 (PVP K-30) denotes as the concentration of X2 increased the disintegration time increased (R^2=1) indicating good correlation between independent and dependant variables.

The parameter percent drug release can be described by model equation

% Drug release = + 62.03 + 3.11 * X1 – 0.6755 * X2

The positive sign for coefficient X1(crosscarmellose sodium) showed percent drug release increased with increase in concentration of X1 and negative sign for X2 (PVP K-30) indicates increased concentration of X2 decreases the percent drug release.

Stability study

The optimized formulation F1 was subjected to stability study as per ICH guidelines. Color, odor, hardness, friability, drug content, disintegration time and percent drug release parameters were evaluated. The optimized formulation did not showed remarkable changes in these parameters (Table 4) and found stable at stability conditions.

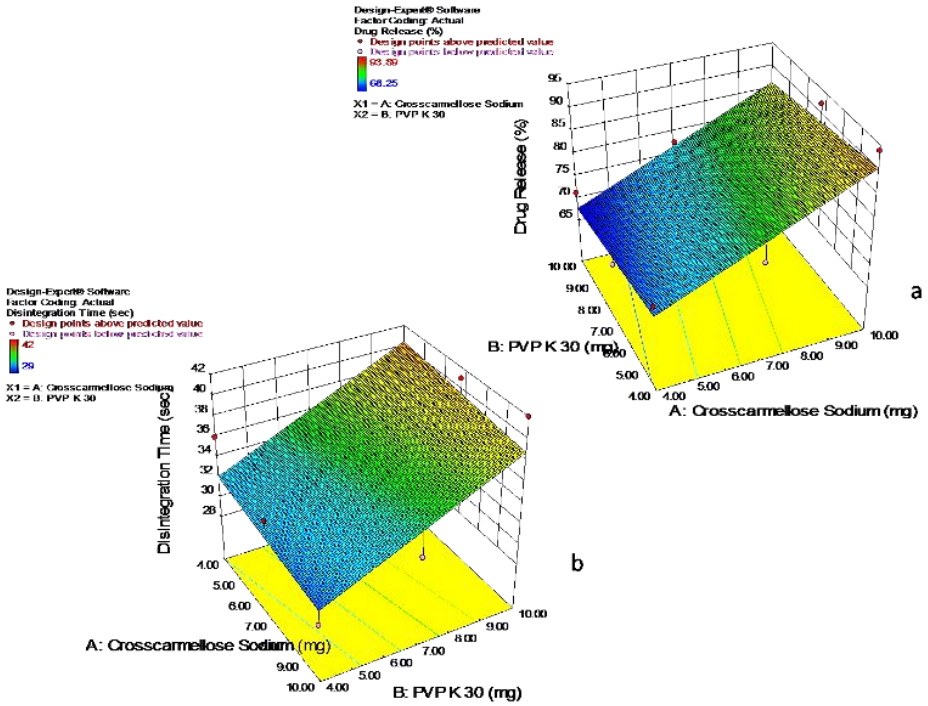

Figure 6. Response surface plots showing the effect of crosscarmellose sodium and PVP K-30

Table 4. Stability study of optimized F1 formulation

Formulation parameter	Ambient condition	30±2º/65±5% RH	40±2º/75±5% RH
Color	white	white	white
Odor	No	No	No
Hardness (kg/cm^2)	3.2±0.80	3.2±0.56	3.3±0.38
Friability (%)	0.84±0.8	0.86±0.34	0.85±0.46
Drug content (%)	99.28±0.3	99.05±0.17	99.14±0.21
Disintegration time(sec)	29±0.15	29±0.67	28±0.11
Percent drug release	93.49±0.11	93.63±0.14	93.39±0.28

Results are expressed as mean±standard deviation (n=3)

Conclusion

The cocrystal of piroxicam was successfully prepared using sodium acetate as guest molecule to improve the solubility and dissolution. Dry grinding method allowed the formation of cocrystals. The cocrystal formation was confirmed by melting point alterations, DSC changes, shifts in Infra Red bands, changes in 2θ values in XRPD and mutually supported each others. The pH solubility profile of piroxicam and its cocrystals showed sigmoidal pattern. The Piroxicam cocrystals exhibited greater dissolution than the pure drug. The directly compressible orodipersible tablets of piroxicam cocrystal with shorter disintegration time, low friability, and greater drug release were developed by 3^2 full factorial design. F1 formulation was found promising based on the evaluation parameters. The result indicated that, selected variables showed significant effect on the responses. Thus piroxicam cocrystals possessing modified physicochemical properties were obtained and successfully formulated as orodispersible tablets.

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Ethical Issues

Not applicable.

Conflict of Interest

The authors declare no conflict of interests.

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JOURNAL CLUB ACTIVITY

Department of Pharmaceutical Chemistry

Attendance cum response sheet for Journal Club of Department of Pharmaceutical Chemistry

Date & Time: 19/08/2020, 2.30pm.

Name of the Facilitator: Dr. Smita Pawar.

Title of the paper discussed: Synthesis, characterization, and anticancer activity of new benzofuran substituted chalcones.

Sr. No.	Name of the member	Signature	Evaluation of today's meeting/suggestions
1.	Mrs. R.S. Chavan	@schavan	The discussion on the chalcones would be useful for pursuing research in the field
2.	Dr. S.J. Pawar	Pawar	Discussion on chalcones as anticancer agent is informative.
3.	Mrs. J.R. Jagtap		very useful discussion Conducted on anticancer activity of Chalcones
4.	Mr. A.P. Kale		Discussion on Synthesis and Biological evaluation of new chemical molecule Benzofuran.
5.	Mr. G. B. Nigade		Anticancer activity of new benfofuran substituted chalcones obtained through this paper.

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Research Article

Synthesis, Characterization, and Anticancer Activity of New Benzofuran Substituted Chalcones

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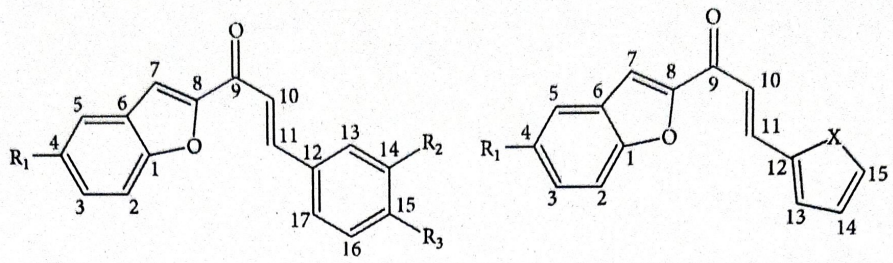
Benzofuran derivatives are of great interest in medicinal chemistry and have drawn considerable attention due to their diverse pharmacological profiles including anticancer activity. Similarly, chalcones, which are common substructures of numerous natural products belonging to the flavonoid class, feature strong anticancer properties. A novel series of chalcones, 3-aryl-1-(5-bromo-1-benzofuran-2-yl)-2-propanones propenones (**3a–f**), were designed, synthesized, and characterized. *In vitro* antitumor activities of the newly synthesized (**3a–f**) and previously synthesized (**3g–j**) chalcone compounds were determined by using human breast (MCF-7) and prostate (PC-3) cancer cell lines. Antitumor properties of all compounds were determined by 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT) assay. Cell viability assay for the tested chalcone compounds was performed and the log IC_{50} values of the compounds were calculated after 24-hour treatment. Our results indicate that the tested chalcone compounds show antitumor activity against MCF-7 and PC-3 cell lines ($p < 0.05$).

1. Introduction

Cancer is one of the most important clinical problems worldwide. Among the wide range of compounds approved as potential anticancer agents, derivatives with functionalities as α,β-unsaturated Michael acceptor have attracted great interest [1, 2]. Previous studies have proposed that anticancer compounds such as alkylating agents bind directly to various cellular nucleophiles, thus lacking selectivity. However, Michael acceptors can be structurally modified so that they can react selectively with target nucleophiles [3]. Chalcones, the compounds having 1,3-diaryl-2-propen-1-one system, also have shown a broad spectrum of biological activities including anti-inflammatory [4–7], antimalarial [8], anti-invasive [9], antibacterial [10–12], and anticancer [13–16] activities. On the other hand, chalcones are capable of inducing apoptosis [17, 18]. Consequently, these compounds are recognized as promising anticancer agents [19–22]. A number of clinically useful anticancer drugs have genotoxic effects because of their interaction with the amino groups of nucleic acids. However, chalcones have been found not to show such undesired side effects [23]. Numerous reports have been published on the interesting anti-breast cancer activity shown by chalcones [24–26]. Benzofuran derivatives are an interesting class of heterocyclic compounds. Benzofuran derivatives are of great interest in medicinal chemistry and have drawn remarkable attention due to their biological activities with chemotherapeutic properties [27]. Some benzofurans bearing various substituents at the C-2 position are greatly distributed in nature; for example, ailanthoidol, a neolignan derivative, has been reported to have antiviral, antioxidant, and antifungal activities [28]. Furthermore, most of the compounds prepared from 2-acetylbenzofuran have antimicrobial, anticancer, antitumor, anti-inflammatory, and antitubulin activities and are also used for treatment of cardiac arrhythmias [29–32]. The use of the combinations of different pharmacological compounds in the design of new drugs may lead to finding novel drugs with interesting biological activity [33, 34]. Furthermore, no studies were found in the literature evaluating anticancer properties of benzofuran substituted chalcone derivatives. This encouraged us to synthesize benzofuran substituted chalcone compounds and to investigate anticancer properties of these compounds.



3a: R_1 = Br, R_2 = H, R_3 = H
3b: R_1 = Br, R_2 = H, R_3 = Br
3c: R_1 = Br, R_2 = NO_2, R_3 = H
3d: R_1 = Br, R_2 = H, R_3 = $N(CH_3)_2$
3i: R_1 = H, R_2 = H, R_3 = H
3j: R_1 = H, R_2 = H, R_3 = $N(CH_3)_2$

3e: R_1 = Br, X = O
3f: R_1 = Br, X = S
3g: R_1 = H, X = O
3h: R_1 = H, X = S

SCHEME 1: Structure of synthetic derivatives **3a–3j**.

In this study, we aimed at designing and synthesizing new compounds (**3a–f**) with both benzofuran and chalcone units in one molecule and examining anticancer activity of this newly synthesized chalcones (**3a–f**) and previously synthesized chalcones [35] (**3g–j**) bearing no substituent in the benzofuran ring as a different series against human breast cancer cell lines (MCF-7) and human prostate cancer cells (PC-3) (Scheme 1).

2. Materials and Methods

2.1. Materials. Chemical agents used in the present study included dimethyl sulfoxide (DMSO; Merck, Germany), penicillin-streptomycin, fetal bovine serum (FBS), and DMEM (Dulbecco's Modified Eagle Medium). Double-distilled water was used at all stages of the experiments. Samples of chalcone compounds for testing were prepared at 1, 5, 25, 50, and 100 μM concentrations.

2.2. Characterization Techniques. Melting points were measured using a differential scanning calorimeter (Shimadzu DSC-50) and were uncorrected. NMR spectra were determined on a Bruker AC 400 (400 MHz) spectrometer, with tetramethylsilane (TMS) as the internal standard in DMSO-d_6 or $CDCl_3$ as solvents. FT-Infrared (FT-IR) spectra were recorded as KBr pellets on a Perkin-Elmer Spectrum One FT-IR spectrometer.

*Synthesis of 1-(5-Bromo-1-benzofuran-2-yl)ethanone (**D1**).* A mixture of 4-bromo salicylaldehyde (1 g, 4.97 mmol) and potassium carbonate (0.69 g, 4.97 mmol) in dry acetone (10 mL) was stirred at 25°C for 1 h. Reaction mixture was cooled at 0–5°C, and then chloroacetone (4 mL, 4.97 mmol) was added dropwise. Reaction mixture was stirred at room temperature for ten minutes and then refluxed. Progress of the reaction was monitored by TLC. Upon completion, the reaction mixture was poured on crashed ice. The precipitated solid was filtered, washed with water, and dried. The product was crystallized from ethanol (yield 1.08 gr, 91%; mp: 117–119°C).

FT-IR (KBr, cm^{-1}). 1667 (C=O), 1542 (C=C); ^{1}H-NMR (400 MHz, DMSO-d_6), ppm: 8.03 (s, 1H, 5-H), 7.82 (s, 1H, 7-H), 7.69 (dd, 1H, J = 8.6 Hz and J = 8.2 Hz, 3-H), 7.65 (d, 1H, J = 8.8 Hz, 2-H), 2.56 (s, 3H, methyl protons); ^{13}C-NMR (400 MHz, DMSO-d_6): 188.40, 154.14, 153.46, 131.43, 129.46, 126.39, 116.63, 114.84, 113.83, 26.97; Anal. Calc.; % C, 50.24; H, 2.95. Found: % C, 50.21; H, 2.99.

*General Procedure for Synthesis of Chalcones (**3a–f**).* A solution of 1-(5-bromo-1-benzofuran-2-yl)ethanone (1 g, 4.18 mmol) and one of the aldehyde derivatives (**2a–f**, 4.18 mmol) in MeOH (10 mL) was cooled at 0–5°C and then 6 mL of aqueous NaOH (1 mol/L) was added to this solution and stirred at room temperature for 3 h. The reaction mixture was poured on crushed ice. The precipitated solid was filtered after neutralization with diluted HCl and was washed several times with water and then dried. The product was recrystallized from ethanol.

*(2E)-1-(5-Bromo-1-benzofuran-2-yl)-3-phenylprop-2-en-1-one (**3a**).* Yield: 70%; M.p. 145–147°C; FT-IR (KBr, cm^{-1}): 1655 (C=O), 1599 (C=C); ^{1}H-NMR (400 MHz, DMSO-d_6), ppm: 8.27 (s, 1H, 5-H), 8.12 (s, 1H, 7-H), 7.92–7.84 (m, 4H, 13-H, 17-H, 10-H, 11-H), 7.84–7.65 (m, 2H, 3-H, 2-H), 7.65–7.40 (m, 3H, 16-H, 15-H, 14-H); ^{13}C-NMR (400 MHz, DMSO-d_6): 178.96, 154.59, 154.55, 144.46, 134.76, 131.63, 131.46, 129.64, 129.50, 129.46, 126.49, 122.18, 116.77, 114.88, 114.56; Anal. Calc.; % C, 62.41; H, 3.39 Found: % C, 62.43; H, 3.43.

*(2E)-1-(5-Bromo-1-benzofuran-2-yl)-3-(3-bromophenyl)prop-2-en-1-one (**3b**).* Yield: 82%; M.p. 206–208°C; FT-IR (KBr, cm^{-1}): 1654 (C=O), 1604 (C=C); ^{1}H-NMR (400 MHz, DMSO-d_6), ppm: 8.29 (s, 1H, 5-H), 8.15 (s, 1H, 7-H), 8.00–7.62 (m, 8H, 3-H, 2-H, 17-H, 16-H, 14-H, 13-H, 10-H, 11-H); ^{13}C-NMR (400 MHz, DMSO-d_6): 178.90, 154.58, 154.52, 143.18, 134.04, 132.47, 131.78, 131.68, 131.43, 129.62, 126.59,

124.98, 122.87, 116.84, 114.98; Anal. Calc.; % C, 50.28; H, 2.48 Found: % C, 50.24; H, 2.50.

*(2E)-1-(5-Bromo-1-benzofuran-2-yl)-3-(3-nitrophenyl)prop-2-en-1-one (**3c**).* Yield: 87%; M.p. 202–204°C; FT-IR (KBr, cm^{-1}): 1666 (C=O), 1610 (C=C); ^{1}H-NMR (400 MHz, DMSO-d_6), ppm: 8.78 (s, 1H, 5-H), 8.37–8.27 (m, 13-H, 15-H, 17-H), 8.13 (s, 1H, 7-H), 8.08 (d, 1H, J = 15.6 Hz, 11-H), 7.92 (d, 1H, J = 16 Hz, 10-H), 7.78–7.68 (m, 3H, 3-H, 2-H, 16-H); ^{13}C-NMR (400 MHz, DMSO-d_6): 178.73, 154.67, 154.40, 148.95, 141.86, 136.66, 135.70, 131.87, 130.92, 129.57, 126.59, 125.43, 124.88, 123.51, 116.85, 115.39, 114.93; Anal. Calc.; % C, 54.86; H, 2.71; N, 3.76 Found: % C, 54.90; H, 2.76; N, 3.75.

*(2E)-1-(5-Bromo-1-benzofuran-2-yl)-3-[4-(dimethylamino)-phenyl]prop-2-en-1-one (**3d**).* Yield: 70%; M.p. 179–181°C; FT-IR (KBr, cm^{-1}): 1646 (C=O), 1579 (C=C); ^{1}H-NMR (400 MHz, DMSO-d_6), ppm: 8.10 (s, 2H, 5-H, 7-H), 7.78–7.56 (m, 6H, 3-H, 2-H, 13-H, 17-H, 10-H, 11-H), 6.77 (d, 1H, J = 2.8 Hz, 14-H), 6.75 (d, 1H, J = 3.6 Hz, 16-H), 3.02 (s, 6H, CH_3); ^{13}C-NMR (400 MHz, DMSO-d_6): 178.52, 155.35, 154.31, 152.75, 145.69, 131.61, 131.10, 129.85, 126.24, 122.00, 116.64, 115.98, 114.83, 112.98, 112.22, 40.56–39.31; Anal. Calc.; % C, 61.64; H, 4.36; N, 3.78 Found: % C, 61.40; H, 3.31; N, 3.80.

*(2E)-1-(5-Bromo-1-benzofuran-2-yl)-3-(2-furyl)prop-2-en-1-one (**3e**).* Yield: 83%; M.p. 170–172°C; FT-IR (KBr, cm^{-1}): 1658 (C=O), 1596 (C=C); ^{1}H-NMR (400 MHz, DMSO-d_6), ppm: 8.03–7.96 (m, 3H, 5-H, 7-H, 15-H), 7.74–7.62 (m, 3H, 3-H, 2-H, 11-H), 7.55–7.40 (d, 1H, J = 15.2 Hz, 10-H), 7.14 (s, 1H, 13-H), 6.71 (s, 1H, 14-H); ^{13}C-NMR (400 MHz, DMSO-d_6): 178.56, 154.54, 154.41, 151.34, 147.15, 131.48, 130.78, 129.65, 126.37, 118.73, 118.50, 116.72, 114.85, 114.57, 113.77; Anal. Calc.; % C, 56.81; H, 2.86 Found: % C, 56.75; H, 2.90.

*(2E)-1-(5-Bromo-1-benzofuran-2-yl)-3-(2-thienyl)prop-2-en-1-one (**3f**).* Yield: 83%; M.p. 168–170°C; FT-IR (KBr, cm^{-1}): 1660 (C=O), 1602 (C=C); ^{1}H-NMR (400 MHz, DMSO-d_6), ppm: 8.17 (s, 1H, 5-H), 8.09 (s, 1H, 7-H), 8.02 (d, 1H, J = 15.6, 11-H), 7.91–7.67 (m, 4H, 3-H, 2-H, 15-H and 13-H), 7.51 (d, 1H, J = 15.2 Hz, 10-H), 7.23 (dd, 1H, 14-H); ^{13}C-NMR (400 MHz, DMSO-d_6): 178.54, 154.53, 154.48, 139.86, 137.27, 134.10, 131.64, 131.54, 129.69, 129.36, 126.42, 120.35, 116.76, 114.90, 114.05; Anal. Calc.; % C, 56.81; H, 2.86 Found: % C, 56.75; H, 2.90.

2.3. *In Vitro Antitumor Activity*

2.3.1. Cell Culture. The cell lines of human breast cancer (MCF-7) and human prostate cancer (PC-3) were employed in our study. The PC-3 and MCF-7 cell lines were retrieved from American Type Culture Collection (ATCC). MCF-7 and PC-3 cells were fed with DMEM medium (supplemented with 4500 mg/L glucose, 10% FBS, 100 U/mL penicillin, and 0.1 mg/mL streptomycin added) in 75 cm^2 culture flasks and RPMI-1640 medium (supplemented 10% FBS, 100 U/mL penicillin, and 0.1 mg/mL streptomycin added), respectively. A humidified carbon dioxide incubator (5% CO_2 + 95% O_2; Panasonic, Japan) was used to keep all cells at 37°C during the experiments. Before the treatment of chalcone compounds, the viability ratios of the cells were identified by 0.4% trypan blue. If the viability ratios were under 90%, we did not initiate the experiments [36].

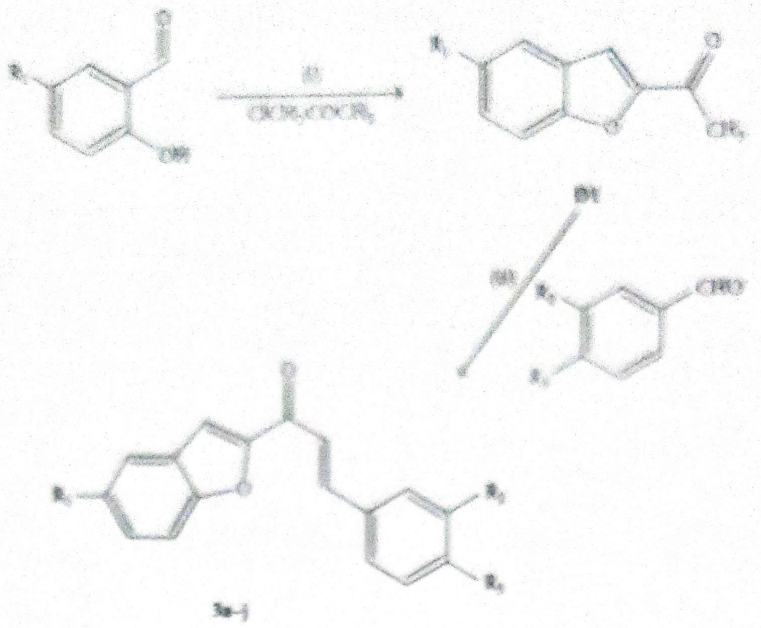
2.3.2. MTT Assay. The synthetic chalcone derivatives were tested for their antitumor activities against different type cancer cell lines (PC-3 and MCF-7) using 3-(4,5-dimethylthiazol–2-yl)-2,5-diphenyl tetrazolium bromide (MTT) assay method. The pale-yellow tetrazolium salt, MTT, was transformed by active mitochondria to form a dark blue formazan that was determined by a microplate reader [37]. The MTT method provides a simple way to detect living and growing cells without using radioactivity.

When the cells were confluent, they were removed from the flasks using trypsin-EDTA solution and were seeded in 96-well plates such that there were 15×10^3 cells in each well. The plates were incubated for 24 h at 37°C. After treatment of these cancer cells with DMSO (for positive control group) and different concentrations (1, 5, 25, 50, and 100 μM) of chalcone compounds (**D1**, **3a–j**) in DMSO, the cells then were incubated for 24 h at 37°C in 5% CO_2 humidified incubator. MTT solution (0.5 mg/mL) was prepared from the MTT stock solution in sterile PBS and was added to each well and the plates were then incubated for 3 h after the incubation for 24 h with chalcone compounds. After that, DMSO and the optical density of the cells were determined by an ELISA reader (Synergy HT, USA) at 550 nm wavelength. The averages of the absorbance values were recorded by reading the control wells that were considered as 100%. The values of absorbance achieved from chalcone compounds and solvent (DMSO) added wells were proportioned to the control values, and the percentages of cell viability were determined. The tests were reiterated ten times at several days [38].

2.4. Statistical Analyses. Quantitative data are expressed as mean ± standard deviation (SD). Normal distribution was confirmed using Kolmogorov-Smirnov test. Quantitative data were analyzed using Kruskal-Wallis H test following Mann-Whitney U test with Bonferroni adjustment as a *post hoc* test. All p values < 0.05 were considered as statistically significant. All analyses were done by IBM SPSS Statistics 22.0 for Windows. The log IC_{50} values were determined by using % cell viability values of compounds by GraphPad Prism 6 program.

3. Results and Discussion

The new 1-(5-bromo-1-benzofuran-2-yl)ethanone was obtained from the reaction of 5-bromosalicylaldehyde and 1-chloroacetone. A series of chalcones (**3a–f**) were synthesized by condensation of 1-(5-bromo-1-benzofuran-2-yl)ethanone and various aromatic aldehydes (**2a–f**) (Scheme 2). For the synthesis of chalcones, the most common route is the base-catalyzed Claisen-Schmidt reaction involving condensation



Scheme 2: General synthesis of benzofuran ketone (DI) with chalcone derivatives (3a–j). Reagents and conditions: (i) K_2CO_3, acetone, reflux; (ii) NaOH, MeOH, rt.

of a benzaldehyde derivative with an acetophenone derivative in methanol with sodium hydroxide catalyst [39–41].

The benzofuran substituted chalcone derivatives (**3a–f**) were characterized by elemental analysis, FT-IR, ^{1}H, and ^{13}C-NMR spectroscopy techniques.

Anticancer activity against MCF-7 and PC-3 was investigated in both these newly synthesized chalcones (**3a–f**) and previously synthesized chalcone derivatives (**3g–j**).

3.1. Structural Characterization. In the FT-IR spectra of 1-(3-bromo-1-benzofuran-2-yl)ethanone, C=O stretching vibration was observed at 1667 cm^{-1}. The synthetic chalcones **3a–f** showed characteristic bands between 1646 and 1666 cm^{-1} (C=O stretching at chalcone) and between 1579 and 1610 cm^{-1} (C=C stretching at chalcone).

The most characteristic signals in ^{1}H-NMR spectra of the benzofuran substituted chalcones were observed at 8.29–8.03 ppm (H-4 at benzofuran ring) and at 7.80–7.40 ppm (*α*-H and *β*-H of chalcone moiety) with a coupling constant about 15 Hz which characterized the transconfiguration of the alkene moiety. The signal of *β*-H was found downfield at a lower field than that of *α*-H due to resonance of *π*-electrons between *α*-carbons and *β*-carbons with carbonyl group. The carbonyl carbon was observed at about 178 ppm in the ^{13}C-NMR spectra of **3a–f**.

3.2. Anticancer Activity. The benzofuran substituted chalcone compounds synthesized were tested for their *in vitro* anticancer activity against two cancer cell lines including MCF-7 and PC-3 at five different concentrations (1, 5, 25, 50, and 100 *μ*M) by MTT assay. The cell viability percentages of tested benzofuran substituted chalcone compounds were determined. Figures 1 and 2 show the effects of the benzofuran substituted chalcones on cell viability measured at 24 h after exposure.

log IC_{50} values of compounds **3a–j** were calculated by using inhibition percentage values by GraphPad Prism 6 program on a computer. log IC_{50} results of this compound are given in Table 1.

The benzofuran substituted chalcones showed anticancer activity on PC-3 and MCF-7 cell lines ($p < 0.05$). All the compounds at 100 *μ*M concentrations significantly reduced the viability percentage of PC-3 and MCF-7 cells ($p < 0.001$).

Table 1: Evaluation of the cytotoxicity and log IC_{50} values (*μ*M) of chalcone compounds and docetaxel (reference chemotherapeutic drug) of two cancer cell lines. log IC_{50} is the concentration of drug that reduces cell growth by 50%.

Compound	MCF-7 log IC_{50} (*μ*M)	PC-3 log IC_{50} (*μ*M)
DI	2.12	1.54
3a	1.89	1.67
3b	1.45	1.24
3c	5.03	6.31
3d	5.79	1.81
3e	0.42	0.67
3f	2.30	2.47
3g	6.43	6.13
3h	2.55	2.57
3i	6.28	6.30
3j	−0.23	0.92
Docetaxel (reference drug)	−0.48	−0.52

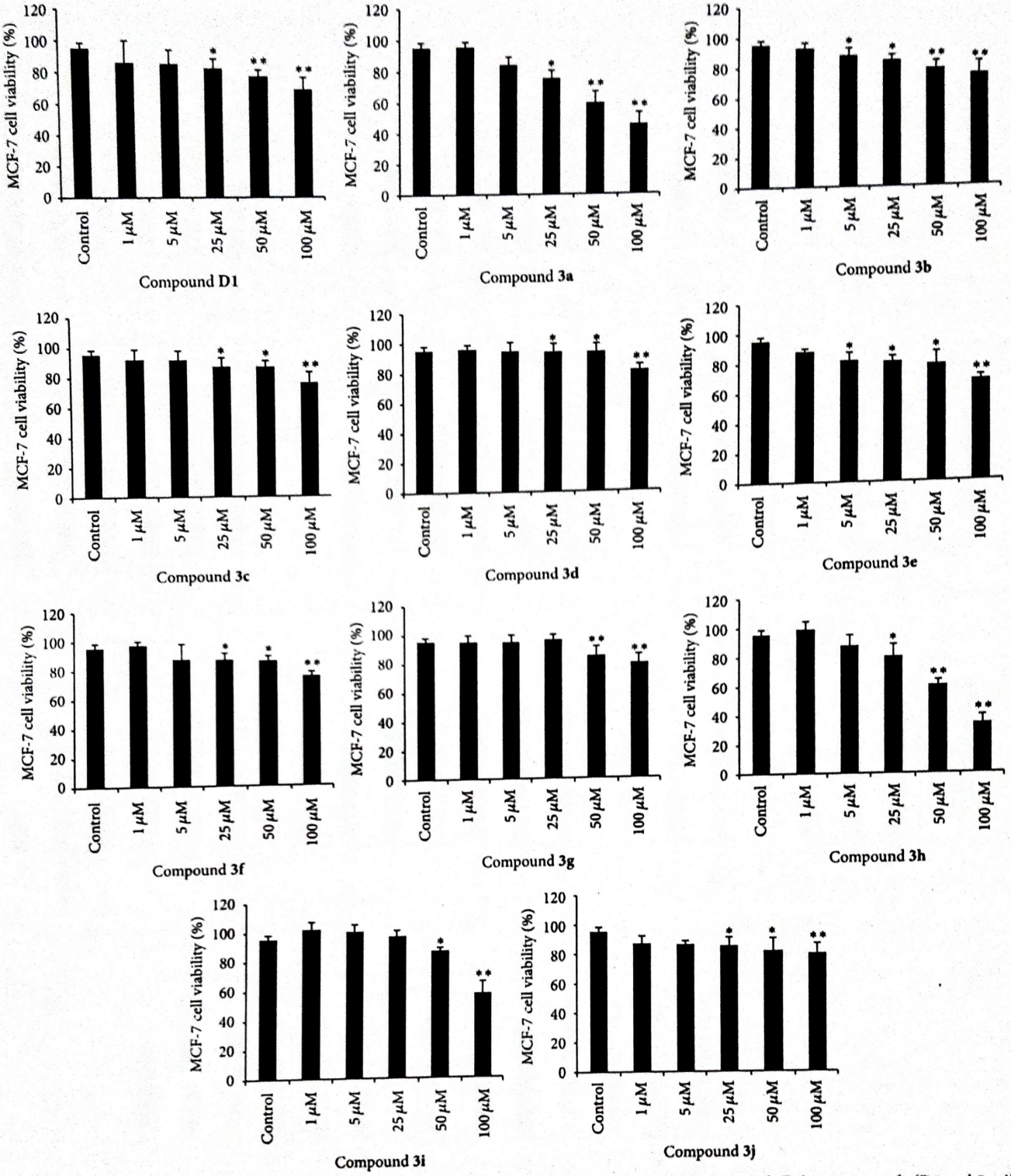


FIGURE 1: The relative cell viability (%) of MCF-7 cells following the exposure of various concentrations of all the compounds (D1 and 3a–j) and untreated control cell for 24 h ($^{*}p < 0.05$; $^{**}p < 0.001$).

Structure activity relationships between these chalcone derivatives and starting material (D1) demonstrated that benzofuran substituted chalcones showed more potent activities than the starting material bearing only an unsubstituted benzofuran ring.

Among the synthesized chalcones, compounds **3a**, **3h**, and **3i** were found to be the most potent against MCF-7 and PC-3 cell lines. In general, chalcone derivatives show anticancer activity. We have not run across any study in literature on the synthesis and anticancer properties of

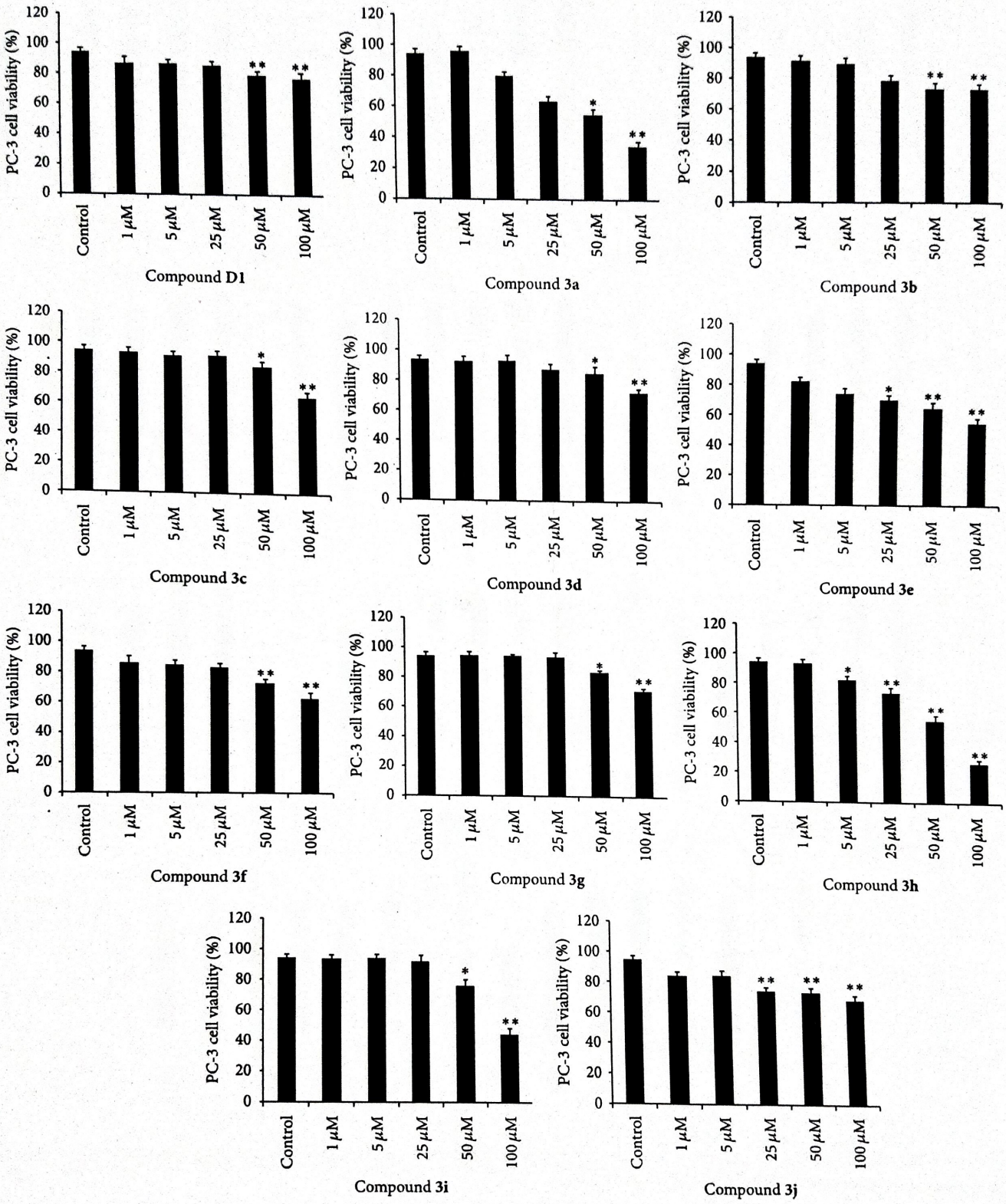


FIGURE 2: The relative cell viability (%) of PC-3 cells following the exposure of various concentrations of all the compounds (D1 and 3a–j) and untreated control cell for 24 h ($^{*}p < 0.05$; $^{**}p < 0.001$).

the chalcone compounds containing benzofuran ring. In this study we have firstly synthesized the chalcone compounds containing benzofuran ring. And also we have firstly studied on the anticancer properties of these compounds. We have studied only MCF-7 and PC-3 cells. These results suggested that benzofuran substituted chalcones could be used as lead compounds to develop novel potent anticancer agents.

4. Conclusions

Synthetic benzofuran chalcone compounds were evaluated *in vitro* for their anticancer activity by MTT assay. The benzofuran substituted chalcone derivatives showed high antitumor activity against MCF-7 and PC-3 cell lines ($p < 0.001$). These results displayed that chalcone derivatives bearing benzofuran ring may be useful in the future for anticancer drug development.

Competing Interests

The authors declare that they have no competing interests.

Acknowledgments

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Name of the Facilitator: P.N. Jagtap

Title of Article: Evaluation of In vitro anti-urolithiatic activity of methanolic extract of C. melo seeds on calcium oxalate crystals.

Sr. No.	Name of the member	Signature	Evaluation of today's meeting/suggestions
1.	Mr. V. C. Shilimkar		Good informative article.
2.	Mrs. P.N. Jagtap		good paper. and good information about cardiotoxicity.
3.	Ms.V.V.Jagtap		Very well informative paper.

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Original Article

EVALUATION OF *IN VITRO* ANTI-UROLITHIATIC ACTIVITY OF METHANOLIC EXTRACT OF *CUCUMIS MELO* SEEDS ON CALCIUM OXALATE CRYSTALS

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ABSTRACT

Objective: This *In vitro* study was carried out to evaluate the anti-urolithiatic activity of the methanolic extract of the *Cucumismelo* seeds on experimentally prepared calcium oxalate crystals which was prepared by the homogeneous precipitation method in the laboratory.

Methods: The crude extract was prepared by the soxhlet extraction method and the extraction was done until all the compounds get extracted into the solution and solvent was evaporated by rotary evaporator. Extracts were stored in an airtight light-resistant container at 4 °C in a refrigerator for further analysis.

Results: Seed extract of *Cucumismelo* showed maximum efficiencies in the dissolution of the calcium oxalate crystals. Cystone drug was used as the standard. This *In vitro* study has shown that the methanolic extract of the seeds of *Cucumismelo* has the potential anti-urolithiatic activity when compared with the standard.

Conclusion: This *In vitro* study has given the primary evidence that the extract of seeds of *Cucumismelo* has the anti-urolithiatic activity. *In vivo* studies can be carried out on the seed extract of *Cucumismelo* for further investigations.

Keywords: Anti-urolithiatic activity, Urolithiasis, *Cucumismelo*, *In vitro*, Methanolic extract

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INTRODUCTION

Stone formation in the human body is the oldest and very painful urologic disorder which forms due to the change in lifestyle and dietary factors. Formation of stones or calculi is called as the lithiasis which approximately occurs 12% of global population. If the stones are formed in the kidney is called as nephrolithiasis and the formation of calculi in the urinary bladder, ureter or anywhere in the urinary tract is known as urolithiasis [1].

The word "Urolithiasis" is derived from Greek as "Urone" for urine and "Lithos" for stones. Urolithiasis is one of the major diseases of the urinary tract with increasing prevalence and incidence in the world. This urologic disorder occurs in approximately 12% of the global population and it is more common in male than female [2]. Its recurrence rate is high 14% after one year, 25%-31.5% after five years, 49%-52% after ten years, 72% after twenty years [3].

This kidney stone formation is a multistep process which is the result from the influences of epidemiological, biochemical and genetic risk factors [4]. The formation of the kidney stones involves several phytochemical events beginning from the crystal nucleation, aggregation, and end with retention within urinary tract [5]. Before the crystal nucleation supersaturation will be take place. Urinary P^H, Ionic strength, Solute concentration and a complexion like factors are affected on the supersaturation process [6].

According to the National Institution of Health of the United State, approximately one person in ten develops urinary stones during their lifetime [7]. Although such data regarding Sri Lanka are not available according to Abeygunasekara 2011[8]. But some studies have suggested a high intake of fluoride act as promoters for the formation of kidney stones. When the fluoride level in drinking water is rise from 3.5 to 4.9 ppm prevalence of urolithiasis is 4.6 times higher than the normal condition. Water wells in dry zone areas in Sri Lanka such as Anuradhapura, Polonnaruwa, and Ampara contain fluoride content greater than 3 ppm.

Treatments for the urolithiasis are varies depending on the composition, location, patient factors and size of the stones in the urinary tract. For the treatments of small calculi can be managed by consuming a considerable amount of drinking water for a day also by treating with the ∝-blockers to flushing out the small stones (Medical expulsion therapy). For the treatment of large stones can be done by using extracorporeal shock wave lithotripsy (ESWL) which break the large stones into tiny pieces. This therapy is high expensive and may damage to the urinary system [9]. Also, they do not prevent the formation of new stones [10].

Using medicinal plants for the treatment of the urolithiasis is not only simple, less side effects but also cost-effective. According to the World Health Organization (WHO) about 70% of global populations are using indigenous medicines to cure various diseases.

Lots of medicinal plants have been using as traditional health care system from the centuries in folk and ayurvedic treatments. Some medicinal plants have been reported which use for the treatments of urolithiasis in folk and ayurvedic medical practices and they have shown a significant effect on *in vitro* and *in vivo* anti-urolithiatic activity in researches which have been done. So, this study was carried out based on the medicinal plants which selected for the evaluation of *in vitro* anti-urolithiatic that have been reported to have anti-urolithiatic property according to the ayurvedic medicinal system in Sri Lanka and in this study calcium oxalate was prepared by mixing calcium chloride dihydrate and sodium oxalate in laboratory condition by homogenous precipitation method. Even though differences between naturally occurring kidney stones and experimentally prepared stones have existed, the study was carried out as an experimental study or as the first step for the drug discovery. If there any significant results are obtained, the study can be proceeded by using stones removed from the patients who affected by the kidney stones.

MATERIALS AND METHODS

Collection of plant materials

The fruits of Cucumismelo were collected in the month of October 2017 from the Thirunelvely local market area and farm areas in kondavil, Jaffna, Sir Lanka. The materials were authenticated by the department of botany, University of Jaffna. The seeds were removed from the strips and

were washed thoroughly with the tap water followed by distilled water. Then seeds were shade dried for three weeks and were pulverized.

Reagents used

Methanol, Sodium oxalate, Tris buffer, Calcium chloride, Potassium permanganate ($KMnO_4$), Conc. Sulphuric acid (H_2SO_4), Mayer's reagent, Wagner's reagent.

Extraction process

Methanolic extract was obtained by using 200g of powdered seeds and using 400 ml of methanol in soxhlet apparatus at 64 °C temperature until all the compounds were extracted into the solvent. The extract was evaporated and concentrated by using rotary evaporator at 45 °C temperature. Further, dried extract was stored in an airtight, light-resistant container at 4 °C in the refrigerator for further analysis [11].

Preparation of calcium oxalate crystals by homogeneous precipitation method

Calcium Chloride dihydrate (4.41g) dissolved in distilled water and Sodium Oxalate (4.02g) dissolved in 2N Sulphuric acid were taken into separate beakers and both solutions were mixed together to react with stirring until Calcium oxalate precipitate formed. Excess Sulphuric acid was removed by washing with Ammonia solution and distilled water respectively. It was allowed to dry at 60 °C for 4 h [6].

Preparation of semi-permeable membranes from farm eggs

The apex of eggs was punctured by a glass rod to remove the entire content. Empty egg shells were washed thoroughly with distilled water and placed in a beaker consisting 2M HCl for an overnight which caused complete decalcification. Then membranes were washed with distilled water and they were placed in ammonia solution for neutralization of acid traces in the moistened condition for a while. Then they were rinsed with distilled water and Stored in a refrigerator at a pH of 7-7.4 [6].

Evaluation of anti-urolithiatic activity by the titrimetric method

Totally 9 semi-permeable membranes were prepared and exactly 5 mg of calcium oxalate crystals and four different concentrations (10 mg, 20 mg, 30 mg, 40 mg) of extracts and standard (Positive control) were placed in separate membranes and they were sutured carefully. One sample which contained calcium oxalate crystals only was used as the negative control. These were allowed to suspend in the separate conical flasks which containing 100 ml of tris buffer solution (0.1M). All the conical flasks were incubated at 37 °C for 7 h. Then the content in the semi-permeable membrane was transferred into a test tube and 2 ml of 1N sulphuric acid was added. The resulting mixture was titrated against the standard KMnO4 solution until the light pink colour was observed. This whole procedure was repeated three times to get the accurate results. The dissolution percentages of the calcium oxalate crystals were calculated for each sample to evaluate the activity [6].

Phytochemical analysis

Chemical tests were carried out on the plant extract using standard procedures to identify the constituent molecules as described by sofowara and co-workers. Aqueous and ethanolic extracts of *Cucumismelo* seeds were prepared. Then phytochemical analysis was carried out on these plant extracts.

RESULTS AND DISCUSSION

The formation of urine stones is a complex process which has several steps such as supersaturation, nucleation, growth, aggregation, and retention [12]. High intake of dietary calcium may inhibit the formation of kidney stones rather than causing the stones [13]. Phytochemicals such as Terpenoids, Tannins, alkaloids, and saponins can be responsible for the anti-urolithiatic activity of the plant extracts. Some phytochemicals which may be effective for the dissolution of the calcium oxalate kidney stones are Kaempferol-3-rhamnoside and Kaempferol-3-rhamnogalactoside, triterpenes such as botulin and tannins [14].

In this study, the anti-urolithiatic activity of the methanolic extract of *Cucumismelo* seeds was compared with the standard drug cystone. Plant extract shows a considerable amount of anti-urolithiatic activity as the standard cystone drug.

The dissolution percentage by the extract of *Cucumismelo* seed at 10 mg, 20 mg, 30 mg and 40 mg concentrations were 67.5(±0.525)%, 77.1(±0.094)%, 80.9(±0.340)%, 85.9(±0.573)% respectively. Dissolution percentage by the standard drug cystone at 10 mg, 20 mg, 30 mg, and 40 mg were found to be as 59.6(±0.432)%, 64.2(±0.163)%, 74.8(±0.283)% and 78.3(±0.249)% respectively. Dissolution percentage for the control test was 22.1(±0.249) %. Phytochemical analysis of the ethanolic and aqueous extracts of the *Cucumismelo* shows the positive results for the presence of alkaloids terpenoids. The research findings revealed that even though cystonepolyherbal drug has high dissolution ability, methanolic extracts of *Cucumismelo* seeds also have considerable anti-urolithiatic activity.

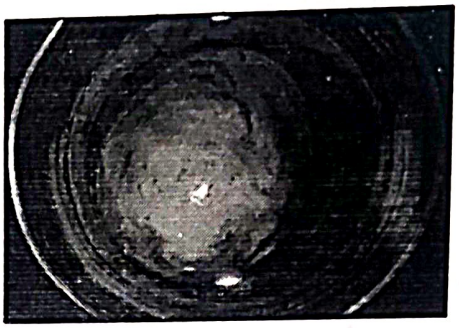

Fig. 1: Decalcified eggs

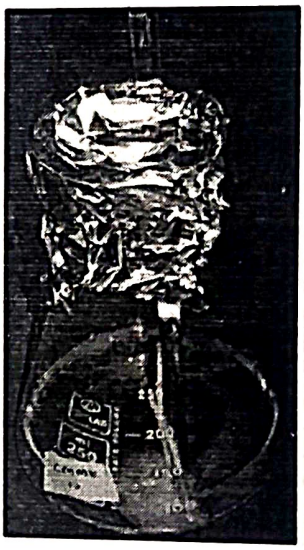

Fig. 2: *In vitro* experimental model setup

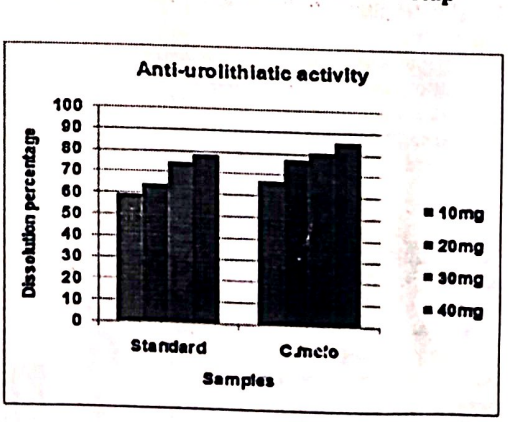

Fig. 3: Anti-urolithiatic activity of the standard and sample

Table 1: Preliminary phytochemical screening

Test name	Aqueous/Ethanolic extract
Mayer's test	+
Wagner's test	+
Saponin	+
Libermann-Budhard's test	-
Phenolic groups	-
Flavonoids	-
Terpenoids	+
Phlobatannin	-

(+) Indicate the presence and (-) Indicate

CONCLUSION

Humankind is known as suffering from urinary stone diseases which are a common and most painful disease found in all around the world. Uses of pashanabheda plants in the treatments of the urinary calculi are most popular in the Ayurvedic and folk medicines. Cucumismelo plant was selected according to the literature found in the Sri Lankan ayurvedic medicines. Methanolic extract of the Cucumismelo seeds has the high anti-urolithiatic activity compared to the standard polyherbal drug cystone. This research work has given the primary evidence for the presence of anti-urolithiatic property of the seeds of Cucumismelo.

ACKNOWLEDGMENT

I am extremely thankful to my research supervisor Dr. R. Srikaran, senior lecturer, Department of chemistry, Faculty of science, University of Jaffna. I am extremely thanks to technical officers, laboratory staff for their kind support. My special thanks to my beloved parents for their blessing and encouragement which helped me lot.

AUTHOR'S CONTRIBUTIONS

All authors have contributed equally

CONFLICT OF INTERESTS

Declare none

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Final B.Pharm (Sem-VIII)
Medicinal Chemistry - IV

Pune District Education Association's

Seth Govind Raghunath Sable College of Pharmacy, Saswad

Trigger1:

Two days ago, Tyler suffered a severe inversion ankle sprain as he landed after going up for a rebound. The team physician was in attendance at basketball practice. After examining Tyler, Dr. Becki gave him Voltaren with instructions for use and dosage. Tyler reports to you that he doesn't feel the medication is doing anything because he still has all the symptoms he had when the injury occurred. You explain to him that because he has been taking it long enough to achieve a steady state of the drug in his system, you will contact Dr. Becki to see if she has suggestions for another nonsteroidal anti-inflammatory drug (NSAID) that may work better for him. How would you explain to Tyler what NSAIDs do therapeutically and why the Voltaren might not have been working?

Pune District Education Association's
Seth Govind Raghunath Sable College of Pharmacy, Saswad.

2020-21
PBL

Class: Final. Y. B. Pharm. (Sem.-VIII))
Subject: Medicinal Chemistry-IV

Sr. No.	Facilitator's Name	Group	Roll number of the students	Name of Group Leader
1.	Dr. Smita Pawar	A	1-10	Bhintade Komal Bhauso
2.		B	11-20	Damare Bharat Rajendra
3.		C	21-30	Jadhav Karishma Prabhakar
4.		D	31-40	Kale Kashmira Sanjay
5.		E	41-50	Khomane Bhagyashri Shrikrushna
6.		F	51-60	Misal Poonam Balasaheb
7		G	61-68	Temgire Pooja Suresh

Pune District Education Association's

Seth Govind Raghunath Sable College of Pharmacy, Saswad.

FACILITATOR's NOTES

Learning Objectives:

1) To learnt about chemistry of NSAIDS.
2) To learn different drugs used in treatment of inflammation and analgesia.
3) To study the side effects of different classes of NSAIDS.

Compilation of:

1. What is NSAIDS?
2. Classify it with examples along with structure.
3. What are side effects of NSAIDS?
4. Give the mechanism of action of NSAIDS.

References:

1) Pharmaceutical Analysis by Dr. A. V. Kasture, Dr. K. R. Mahadik, Dr. S. G. Wododkar & Dr. H. N. More, Nirali Prakashan, Volume I, Page No.-9.1-9.10.
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Pune District Education Association's

Seth Govind Raghunath Sable College of Pharmacy, Saswad.

FACILITATOR ASSESSMENT FORM

PBL No.: 1 **Date:**

Subject: Medicinal Chemistry - IV **Class:** Final B. Ph (Sem-VIII)

Please rate in the 5 point scale: 5- Excellent, 4- Very Good, 3- Good, 2- Satisfactory, 1 - Not satisfactory

Criteria \ Roll No. of the student	1	2	3	4	5	6	7	8	9	10
Application of knowledge base										
Applies previous knowledge to clarify and define the problem.	2	3	3	3	3	2	3	3	2	
Answers questions and shares his/her opinions by applying acquired knowledge.	2	3	3	2	2	3	3	3	3	
Critical Thinking						2				
Demonstrate, evidence, critical understanding and critical analysis facts.	3	3	3	3	3	2	3	3	2	
Is applicable making conclusion and decision regarding the diagnostic / therapeutic approaches?	2	4	3	2	2	3	3	3	2	
Demonstrates evidence of following a sequential analysis of the problem.	2	3	3	3	3	2	3	3	3	
Self Directed Learning(Self study)										
Defines learning objectives and learning goals.	3	4	3	3	3	2	3	3	2	
Demonstrates evidence of accomplishment of learning objectives.	3	4	4	3	3	2	4	4	3	
If necessary, seeks counseling to orient His/her study and willing to improve	3	4	4	3	3	3	3	3	2	
Collaborative work										
Works towards achievement of the groups learning goals with commitment.	2	3	4	4	2	2	3	4	3	
Demonstrates effective interpersonal attributes.	2	4	4	4	2	3	4	4	3	
Accepts feedback with openness.	3	4	4	4	3	3	3	4	3	
Reacts positively to feedback and criticism.	3	4	3	4	2	3	4	4	3	
Stands up for his/her points of view.	2	4	4	3	2	3	4	4	3	
Shows ability to change his/her point of view of new information given/ obtained.	2	4	4	4	3	2	4	4	3	

Pawar

Signature of Facilitator

(Dr S.T. Pawar)

Pune District Education Association's
Seth Govind Raghunath Sable College of Pharmacy, Saswad

Feedback of students on PBL conducted on 29/04/2021.

Subject: **Class:**

This questionnaire has been designed to understand the opinion of students involved in the PBL activity so that the activity can be improved in the future. The group leader is advised to answer the questions on behalf of all the group members.

Please **tick** the appropriate box:

Trigger	Yes	No	Can't say
Was the trigger provided to you easily understandable?	✓		
Was the trigger interesting?	✓		
Could you relate the trigger to your curriculum?	✓		
Role of facilitator			
Did you find the role of facilitator useful in understanding the problem?	✓		
Did you take the help of the facilitator in identifying the objectives of the problem?	✓		
Resources			
Did you refer to the books available in the library for compiling the data related to your problem?		✓	
Were there sufficient reference books available in the library for researching the problem?	✓		
Did you find the internet facility and online resources adequate?	✓		
Overall activity			
Do you think PBL is enhancing your comprehension and analytical skills?	✓		
Do you think PBL is enhancing your referencing & researching skills?	✓		
Do you think PBL is contributing towards improving your communication and presentation skills?	✓		
Do you think this activity should be continued in future also?	✓		

Suggestions if any,---Very nice activity

---Pl. tear from here before submitting---

Name of the group leader...Samiksha Bhongale.....Signature.....

Group No.:

Pune District Education Association's
Seth Govind Raghunath Sable,
College of Pharmacy, Saswad.

subject :- Medicinal Chemistry - IV
Problem Based Learning (PBL)
(Group - I)

Sr. No.	Sr. No.	Name of the students.	sign.
	1.	Agawile Praikta Nitin (scriber)	Agawile
	2.	Atre Prathmesh Suhas (Reader)	ATS
	3.	Bankar Supriya Prakash	Sbankar
	4.	Bhagat Akash Sanjay	Abhagat
	5.	Bhalerao Shivkumar shankarrao	Sbhalerao
	6.	Bhapkar Suraj Jaysing	SB
	7.	Bhintade Komal Bhausо	PBK
	8.	Bhongale samiksha sambhaji (Leader)	Sbhongale
	9.	Bhosale Prashant Sanjay	Bhosale
	10.	Borade Gaurav Raihans	Sborade

NSAID's Possess anti-Inflammatory and analgesic effects. In the case of a sprain such as this, an NSAID would decrease the pain and inflammation associated with the injury. However, you should always remember that NSAID's, like all other medications, have adverse effects. In particular, the athlete should be aware of the potential for GI adverse effects from use of NSAIDs. There is significant individual variation in response to NSAIDs. Some patients will not respond to one NSAID but another agent in the same class will have appropriate therapeutic benefit. This individual variation is likely the reason why the voltaren was not working for Tyler. Contracting the physician about a different NSAID would be appropriate in this case. You should also rule out nonadherence to the medication regimen as a potential cause of the poor response.

NSAIDs :-

Nonsteroidal anti-inflammatory drugs are members of a drug class that reduces pain, decreases fever, prevents blood clots and in higher doses, decreases inflammation.

Classification of NSAIDs :-

A] Nonselective COX inhibitors :-

1. Salicylates :- Aspirin
2. Propionic acid derivatives : Ibuprofen, Naproxen

3. Aryl-acetic acid derivatives
e.g. Diclofenac.

4. oxicam derivatives :- Piroxicam

5. Pyrrolo - Pyrrole derivative : Ketorolac

6. Indole derivative :- Indomethacin.

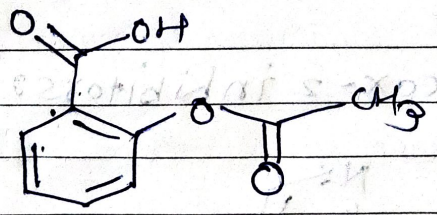
B] Preferential COX-2 inhibitors :-
meloxicam, Nabumetone.

C] Selective COX-2 inhibitors :- Celecoxib.

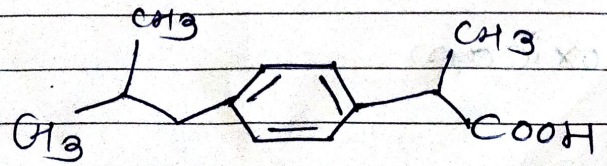
D] Analgesic - antipyretic with poor anti inflammatory action Paraamino-phenol derivative :- Paracetamol (Acetaminophen).

Structure of Drugs :-

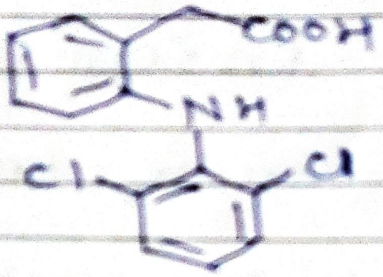
1) Salicylate : e.g. Aspirin



2) Propionic acid drivatives : Ibuprofen

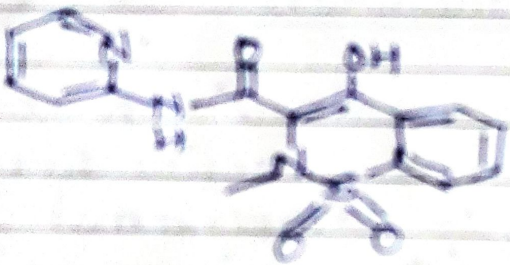


3) Diclofenac :-

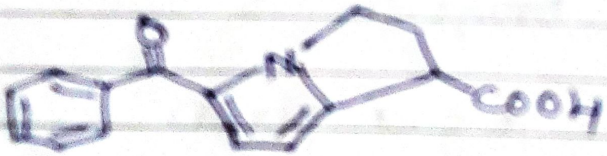


2-[2-(2,6-dichloroaniline)Phenyl] acetic acid

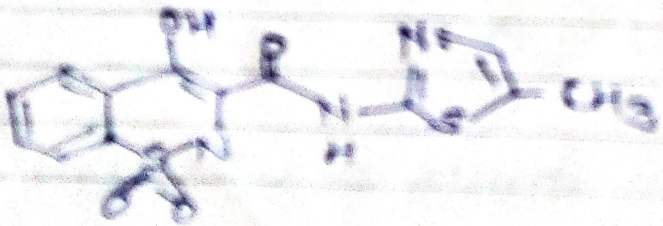
4] Piroxicam



5] Ketorolac :-

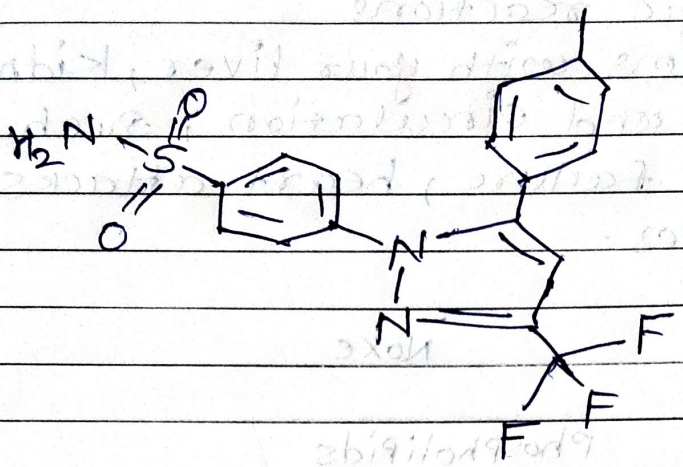


6] Preferential cox-2 inhibitors :-

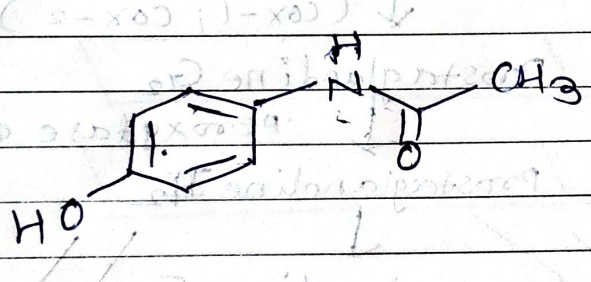


Meloxicam

C] selective COX-2 inhibitors :-
Celecoxib :-



D] Analgesic :- Paracetamol.



Side effects of NSAID :-

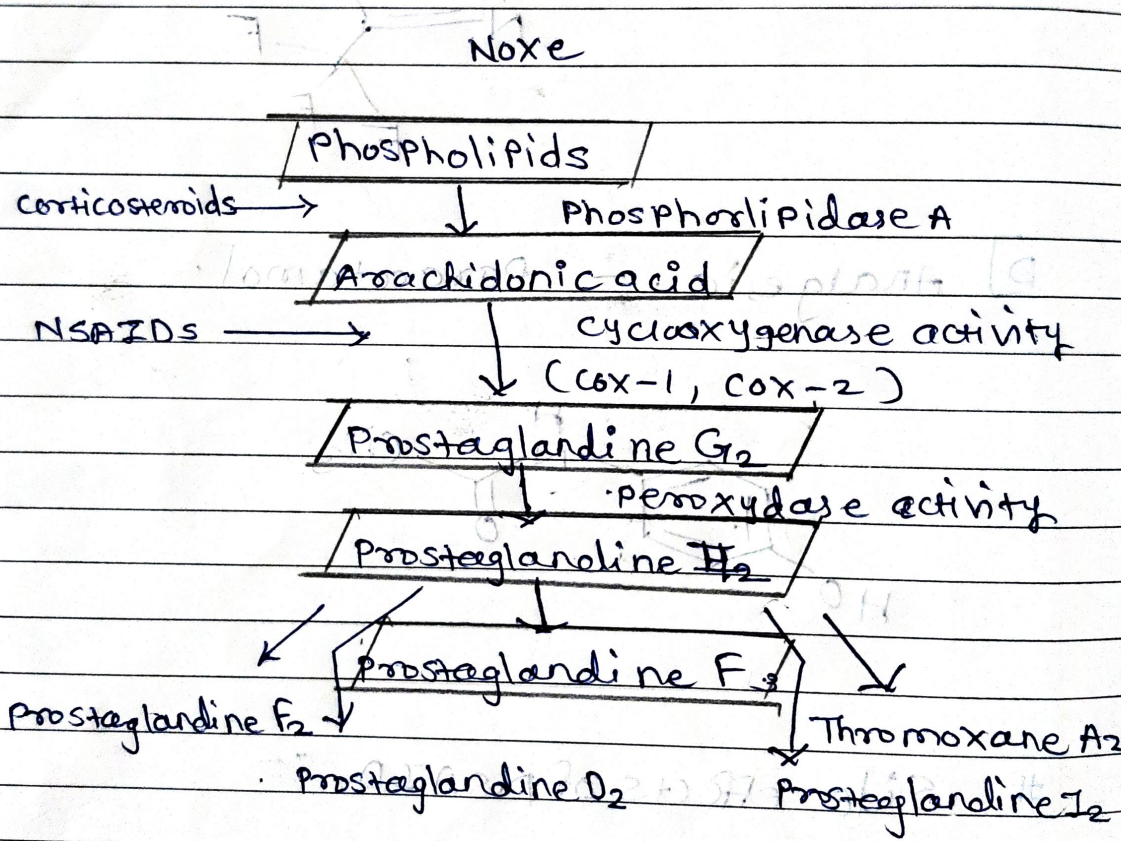
Possible side effects of NSAID's include :-

1) Indigestion - including stomach aches, feeling sick & diarrhoea

2) Stomach ulcers - these can cause internal bleeding and anaemia, extra medicine to protect your stomach may be

prescribed to protect your stomach may be prescribed to help reduce this risk.

3) headaches
4) drowsiness
5) allergic reactions
6) problems with your liver, kidneys or heart and circulation, such as heart failure, heart attacks and strokes.



Trigger

PBL

Pharmaceutical Analysis- VI

Final.Yr.B.Pharm

HPLC method development has been improved by advances in column technology and instrumentation, problems still arise. Systematic means of isolating, identifying, and correcting many typical problems. The important segments of an HPLC system are the same, whether you use a modular system or a more sophisticated unit. Problems affecting overall system performance can arise in each component. Some common problems such as Peak shape, Ghost peak, Column condition & flow rate.

FACILITATOR's NOTES

Learning objectives:

1. To know Trouble shooting.

2. To understand problem affecting to HPLC

3. To know about peak shape.

4. Application of flow rate

5. To understand about column conditions

Compilation of:

1. Knowledge about column Temperature.

2. Information about Peak tailing.

3. Information about Ghost peak.

4. Understanding of Flow rate.

References:

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Pune District Education Association's

Seth Govind Raghunath Sable College of Pharmacy, Saswad.

FACILITATOR ASSESSMENT FORM

Subject: Pharmaceutical Analysis IV

Please rate in the 5 point scale: 5- Excellent, 4- Very Good, 3- Good, 2- Satisfactory, 1 - Not satisfactory

Roll No. of the student / Criteria	01	02	03	04	05	06	07	08	
Application of knowledge base									
Applies previous knowledge to clarify and define the problem.	4	3	3	4	4	4	3	4	
Answers questions and shares his/her opinions by applying acquired knowledge.	3	4	4	4	3	4	4	4	
Critical Thinking									
Demonstrate, evidence, critical understanding and critical analysis facts.	3	4	4	4	4	3	4	4	
Is applicable making conclusion and decision regarding the diagnostic / therapeutic approaches?	4	4	4	3	4	4	3	3	
Demonstrates evidence of following a sequential analysis of the problem.	4	3	3	4	3	4	3	4	
Self Directed Learning(Self study)									
Defines learning objectives and learning goals.	4	3	4	4	3	4	4	3	

Demonstrates evidence of accomplishment of learning objectives.	3	4	3	4	4	3	4	4	
If necessary, seeks counseling to orient His/her study and willing to improve	4	3	4	4	4	3	4	3	
Collaborative work									
Works towards achievement of the groups learning goals with commitment.	3	3	4	4	4	4	4	4	
Demonstrates effective interpersonal attributes.	3	4	3	4	4	3	4	4	
Accepts feedback with openness.	4	3	3	4	4	3	4	3	
Reacts positively to feedback and criticism.	4	3	4	4	4	3	4	4	
Stands up for his/her points of view.	3	4	4	3	4	4	4	4	
Shows ability to change his/her point of view of new information given/ obtained.	4	3	3	4	4	4	3	4	

Bhosale

Signature of Facilitator

(N.A. Bhosale)

Pune District Education Association's
Seth Govind Raghunath Sable College of Pharmacy, Saswad

Feedback of students on PBL conducted on **06/10/2020**

Subject: Pharmaceutical Analysis V **Class:** Final Yr. B.Pharm.

This questionnaire has been designed to understand the opinion of students involved in the PBL activity so that the activity can be improved in the future. The group leader is advised to answer the questions on behalf of all the group members.

Please **tick** the appropriate box:

Trigger	Yes	No	Can't say
Was the trigger provided to you easily understandable?	✓		
Was the trigger interesting?	✓		
Could you relate the trigger to your curriculum?	✓		
Role of facilitator			
Did you find the role of facilitator useful in understanding the problem?	✓		
Did you take the help of the facilitator in identifying the objectives of the problem?	✓		
Resources			
Did you refer to the books available in the library for compiling the data related to your problem?	✓		
Were there sufficient reference books available in the library for researching the problem?	✓		
Did you find the internet facility and online resources adequate?	✓		
Overall activity			
Do you think PBL is enhancing your comprehension and analytical skills?	✓		
Do you think PBL is enhancing your referencing & researching skills?	✓		
Do you think PBL is contributing towards improving your communication and presentation skills?	✓		
Do you think this activity should be continued in future also?	✓		

Suggestions if any,----------
We Understood about troubleshooting.

----------Pl. tear from here before submitting----------

Name of the group leader..Atre Prathmesh....Signature.....

Group No.: 01

DATE 06 10 20

PBL

subject - Pharmaceutical Analysis.

class - Final year. B.Pharm (Sem-VII)

06/10/2020

Roll No.		Sign.
1.	Agawile Prajakta N.	
2.	Atre Prathmesh S	
3.	Bankar Supriya P	
4.	Bhagat Akash S	
5.	Bhalerao Shivkumar S	
6.	Bhapkar Suraj T.	
7.	Bhintade Komal B.	
8.	Bhongale Samiksha S.	

1) Peak tailing -

- Peak tailing has been the most common peak shape problem since the early days of RP-HPLC.
- Most peak tailing is due to interection with acidic or ionized silanol groups on the surface of the sillica particles within the coloumn.
- The low-purity sillica often called Type "A" or acidic sillica has high content of acidic silanol (-si-OH) groups and the presence of metal impurities (especially iron and aluminium) further increases the ionization of these groups to -si-O^- which provides cation exchange sites.
- Silanol tailing is best reduced by using a high-purity sillica coloumn, but there are other techniques to reduce tailing.
- TEA is a very effective competitor for acidic silanol groups but with today's high-purity sillica, TEA is not needed & is rarely used.

2) Flow rate problems -

- Flow rate problem can be due to bubbles, leaks or pump problems.
- with two headed pumps, the flow and pressure may pulse if a bubble is present in only one pump head.
- Leaks also will increase retention times.

- Look for dripping fittings or crystalline deposits on fittings or crystalline as evidence of leaks.
- Pay special attention to fittings upstream from the column.
- Fitting and seals inside the autosampler may be hard to inspect - a flashlight and small mirror can be helpful.
- If stainless steel fittings are in use usually a 1/4 turn of the fitting nut will stop a leak.
- With peak fittings, it is best to stop the pump loosen the fitting, push the tubing to the bottom of the fitting port & then tighten the fitting prior to restarting the pump.
- Tightening a PEEK fitting with the flow on may cause the tubing to slip in the fitting, creating extra-column volume, which can degrade the seperation.

3) Column Temperature -

- column temperature is a useful tool for lowering the system pressure in reverse phase HPLC. through lowering the viscosity of the mobile phase.
- Use of higher temperature can enable increased flow rates & mobile phase mixes that might not otherwise be possible at 25 C because pressure

becomes to great.
- Higher temperatures usually leads to components eluting more quickly which can also sharpen up peaks that have otherwise have relatively long retention times on the flipside at higher temperature.

*) Ghost Peaks -
- Late elution of peaks from a previous run can appear as unexpectedly broad peaks in isocratic seperation.
- For isocratic seperations, the longer the retention time, the broader the peak should be, but all peaks in a narrow region of the chromatogram should have approximately the same peak width.
- Ghost peaks in gradient runs can be isolated by running a non-injection blank gradient and observing the baseline.
- When an excessive number of peaks appear in the blank gradients, dirty reagents are ~~only~~ one likely cause of the problem.
- In this case, the peaks in the run of figure are quite small (1-3 mAU) & would be of little concern for a major component assay of peaks in the 0.8-1.0 mAU size range may require qualifications. In such cases further investigation is warranted:

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PBL - Trigger

Class :- S.Y. B.Pharm (Sem-IV) Date :- 24/05/2021

Subject :- Physical pharmaceutics-II

Group participant :-

Roll No.	Name
21.	Jadhav Vaishanvi Shivaji
22.	Jagtap Sahil Sunil
23.	Javalkar Aditya Hanumant
24.	Kale Sakshi Ravindra
25.	Kande Tanuja Kondiba
26.	Kawade Anagha Avinash
27.	Khaire Mayuri Sunil
28.	Khaire Yogita Shailesh
29.	Khaladkar Ruta Vinayak
30.	Kharat Akash Bhagwanrao

1. Information about particle size determination.

Ans. Many method available for determing particle size such as optical microscopy, sieving, sedimentation and particle volume measurement.

1. optical microscopy (range: 0.2-100 μm).
2. sieving (range 40-9500 μm).
3. sedimentation (range 0.08-300 μm).
4. particle volume measurement (range: 0.5-300 μm)

Range of particle sizes.

A guide to range of particle sizes applicable to each method is

particle size	Method.
1 m	Electron microscope, ultracentrifuge, adsorption
1-100 m	optical microscope, sedimentation, coulter counter, air permeability
50 m	sieving.

- optical microscopy :.

(range : 0.2-100 μm)

The microscope eyepiece is fitted with a micrometer by which the size of the particles may be estimated.

- According to the optical microscopic method, an emulsion or suspension is mounted on ruled slide on a mechanical stage
- The microscope eyepiece is fitted with a micrometer by which the size of the particles can be estimated.
- the ordinary microscope used for measurement the particle-size in the range of 0·2 to about 100 μm.

– Disadvantage of microscopic method

1. The diameter is obtained from only two dimension of the particle
2. The number of particle that must be counted (300-500) to obtained a good estimation of the distribution makes the methad somewhat slow and tedious

– sieving

(range :- 40-9500 μm)

- standard size sieves are available to cover a wide renge of size
- these sieves are designed to sit in a stack so that material falls though smaller and smaller meshes until it reaches a mesh which is too fine for it to pass through
- The stack of sieves is mechanically shaken to promote the passage of the solids
- The fraction of material b/w pairs of sieve sizes is determined by weighing the residue on each sieve

- The result achieved will depend on the duration of agitation and the manner of agitation

– Disadvantages of sieving method.

1. sieving errors can arise from number of variables including sieve loading duration and intensity of agitation
2. clogging of sieves affect the result.

– sedimentation

(range :- 0.08-300 μm)

- By measuring the terminal settling velocity of particles through a liquid medium in a gravitational centrifugal environment using Andreasen apparatus.

2. understanding of diffrent types of diameters :-

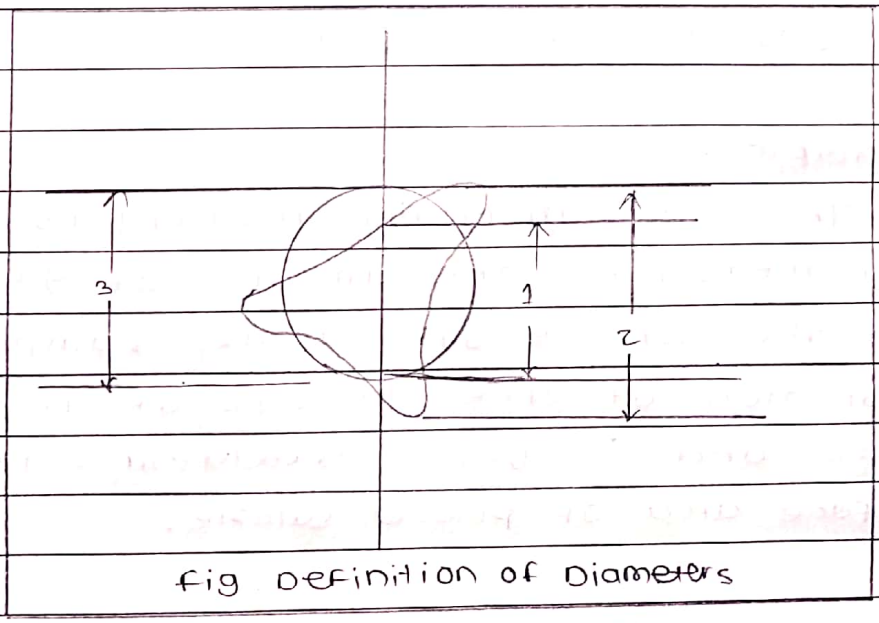


fig Definition of Diameters

1. Martin's Diameter :-

It is the length of line that bisects the particle image. The line may be drawn in any direction but must be in the same direction for all particles

2. ferets Diameter :- It is the distance b/w two tangent on opposite sites of particles parallel to same fixed direction

3. projected area diameter :-

It is the diameter of circle with same area as that of the particle observed perpendicular to surface on which the particle rests.

3. Information about Gas adsorption method.

This method is depending on adsorption of gas on particle surface

principle :-

The gas adsorption method is a method for measuring the amount of gas adsorbed on the surface of powder sample as a function of the pressure of the adsorbate gas and is used to determine the specific surface area of powder sample.

measurement are usually performed at the boiling

point of liquid nitrogen (-196°c)

When the gas is physically adsorbed by the powder sample, the following relationship holds:-

$$\frac{P}{y(P_o - P)} = \frac{1}{y_m b} + \frac{b-P}{y_m b} \cdot \frac{P}{P_o}$$

where

P : partial vapour pressure of adsorbate gas in equilibrium (KPa)

P_o = saturated pressure of the adsorbate gas at -196°C (KPa)

y = volume of gas adsorbed at equilibrium (ml)

y_m = The mass of gas that 1 gram of solid adsorption can take up when monolayer is completed

b = constant, proportional to heat of adsorption and latent heat of condensation of subsequent layers

This equation is called BET equation

The specific surface area s is determined From y_m, the volume of gas adsorbed in a monolayer on the sample

$$S = \frac{y_m \times N \times a}{m \times 22400}$$

where,

S = specific surface area (m_2/g)

N = Avogadro constant

a = Effective cross-sectional area of one adsorbate molecule (m_2)

m = mass of the test powder (g)

specific surface area is generally expressed in units of m_2/g.

PBL -1 TRIGGER

Class: Final Year B. Pharm. (Sem-VII) **Subject: Pharmacology–IV**

LJ, a 57-year-old man with bipolar disorder, comes to a psychiatric clinic for routine follow-up. He has been taking lithium for a few years and states, "I never miss a dose." During the visit, LJ complains of fatigue, some gastrointestinal distress, and a new hand tremor. A lithium level is drawn, and LJ is found to have an elevated level of 1.5 mEq/L. Exhausting other explanations, the clinic staff calls LJ's community pharmacy to determine if a drug interaction may have been the cause of the elevated lithium level. The pharmacist checks LJ's profile and discovers the only recent change in his medications was the addition of hydrochlorothiazide to treat newly diagnosed hypertension.

Group No : A(Roll no-1-10)

Facilitators Name : Prof P. N.Jagtap

Date-26/3/2021

Group A leader : Supriya Bankar.

FACILITATOR's NOTES

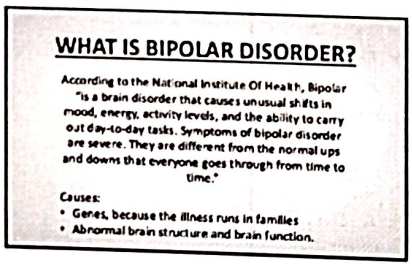
Learning objectives:

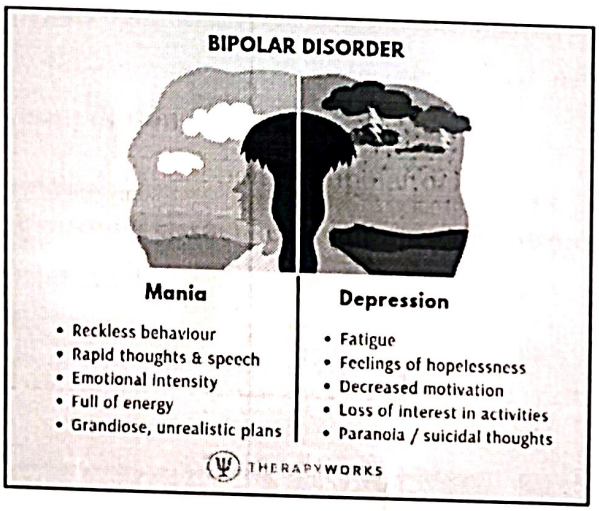
- To explain bipolar disorder.
- To explain the role of lithium.
- To understand drug drug interaction

Compilation of:

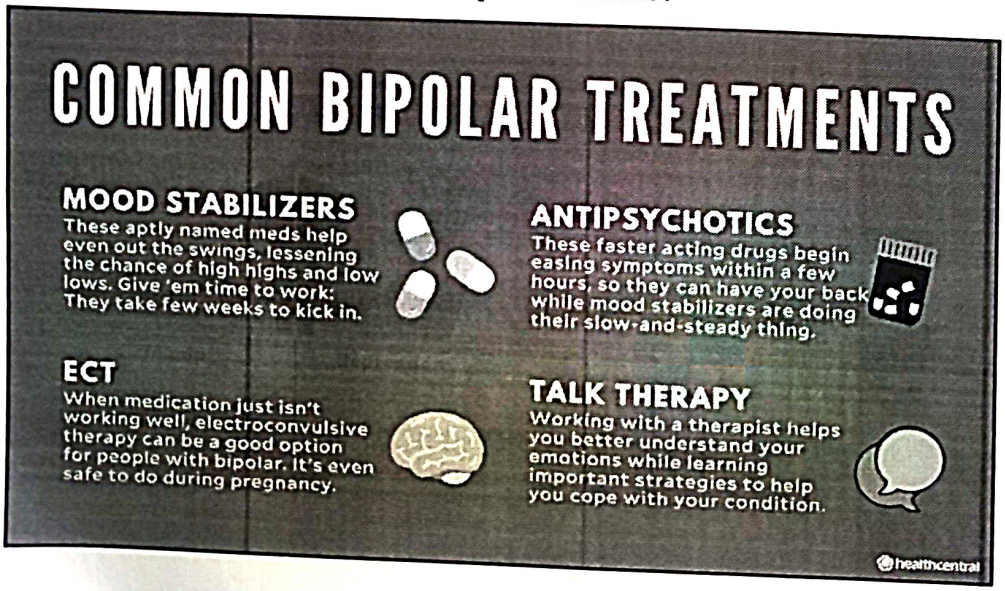
1. Introduction of Bipolar disorder :

A disorder associated with episodes of mood swings ranging from depressive lows to manic highs.





2. What is treatment for the bipolar disorder?



Psycological therapies

Lifestyle changes

prescription medications

Medications

- Treatment of bipolar disorder involves three therapeutic domains: acute mania, acute depression, and maintenance.
- Lithium
- Antiepileptic drugs: divalproex, carbamazep and lamotrigine
- Antipsychotic drugs: olanzapine, risperidone, and quetiapine
- Used alone or in combination, are increasingly being used successfully to treat acute mania and to maintain mood stability (McIntyre, 2004).

3. What is the nature of the interaction between hydrochlorothiazide and lithium?

Lithium + Thiazide interaction

Probable mechanism:

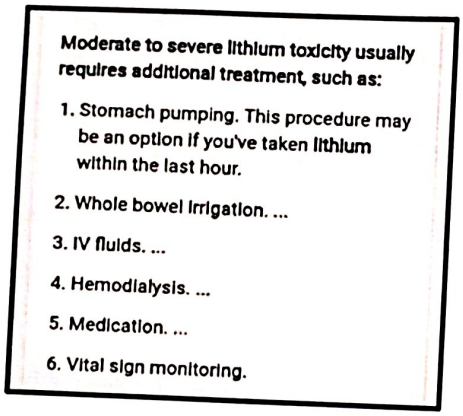
- Thiazides cause diuresis and initial sodium loss.
- Compensatory sodium retention in proximal tubules.
- Proximal tubules do not distinguish sodium from lithium.
- Lithium also retained and accumulates.

Pharmacokinetic Drug Interactions

The level of lithium is elevated in the blood by interacting with hydrochlorthiazide

What might happen: Your blood levels of **lithium** may increase and cause toxic effects such as nausea, vomiting, diarrhea, drowsiness, loss of appetite, muscle weakness, slurred speech, trembling, blurred vision, confusion, seizures, dizziness, or increased urination.

4. How could this interaction be handled?



Lithium level is **elevated** due to interavtion with **Hydrochlorthiazide** hence its this both drugs should not be prescribed together.

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Feedback of students on PBL conducted on 26/03/2021

Subject: Pharmacology V **Class:** Final Year B.Pharm

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Please **tick** the appropriate box:

Trigger	Yes	No	Can't say
Was the trigger provided to you easily understandable?	☑		
Was the trigger interesting?	☑		
Could you relate the trigger to your curriculum?	☑		
Role of facilitator			
Did you find the role of facilitator useful in understanding the problem?	☑		
Did you take the help of the facilitator in identifying the objectives of the problem?	☑		
Resources			
Did you refer to the books available in the library for compiling the data related to your problem?	☑		
Were there sufficient reference books available in the library for researching the problem?	☑		
Did you find the internet facility and online resources adequate?	☑		
Overall activity			
Do you think PBL is enhancing your comprehension and analytical skills?	☑		
Do you think PBL is enhancing your referencing & researching skills?	☑		
Do you think PBL is contributing towards improving your communication and presentation skills?	☑		
Do you think this activity should be continued in future also?	☑		

Suggestions if any,---NO.---

---Pl. tear from here before submitting---

Name of the group leader : **Supriya**

Bankar.....Signature.....

Group No.: **A**

Pune District Education Association's
Seth Govind Raghunath Sable College of Pharmacy, Saswad.

2020-2021

PBL -1 TRIGGER

Class: Third Year B. Pharm. (Sem-V) **Subject: Pharmacology–II**
Date: 03/12/2020

You are the nurse working in an anticoagulation clinic. One of your patients is Kakade A.N., who has a long-standing history of an irregularly irregular heartbeat (atrial fibrillation, or A-fib) for which he takes the oral anticoagulant warfarin (Coumadin). Recently, Kakade had his mitral heart valve replaced with a mechanical valve.

The health care provider does a brief focused history and physical examination, orders additional lab tests, and determines that there are no signs of bleeding other than the nosebleed, which has stopped. The provider discovers that Kakade recently went to the local urgent care center for a sinus infection and had received a prescription for the antibiotic co-trimoxazole (sulfamethoxazole-trimethoprim)

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2020-2021

FACILITATOR's NOTES

Learning objectives:

1. To learn how to do case studies and its detailed problem solving.
2. To learn about the anticoagulant activity and drug involve in it.
2. To learn about anticoagulant and antibiotic drug-drug interaction.

Compilation of:

1. How does atrial fibrillation differ from a normal heart rhythm?
2. What is the purpose of the warfarin (Coumadin) in Kakade's case?
3. What is a PT/INR test, and what are the expected levels for Kakade? What is the purpose of the INR?
4. What happened when Kakade began taking the antibiotic?
5. What should Kakade have done to prevent this problem?

References:

a. Tripathi KD. Essentials of Medical Pharmacology. 7th edition, Jaypee Brothers Medical Publishers (P) Ltd. Page Nos.160-169.

Pune District Education Association's
Seth Govind Raghunath Sable College of Pharmacy, Saswad.

FACILITATOR ASSESSMENT FORM

PBL No.: 1 **Subject: Pharmacology–II**
Class: Third Year B. Pharm **Date: 03/12/2020**
Please rate in the 5 point scale:
5- Excellent, 4- Very Good, 3-Good, 2- Satisfactory,
1 - Not satisfactory

Criteria / Roll No. of the student	41	42	43	44	45	46	47	48	49	50
Application of knowledge base										
Applies previous knowledge to clarify and define the problem.	5	5	5	4	5	5	4	5	5	5
Answers questions and shares his/her opinions by applying acquired knowledge.	4	4	4	5	5	5	5	5	4	4
Critical Thinking			5				5	4	4	5
Demonstrate, evidence, critical understanding and critical analysis facts.	5	5	5	4	4	4	4	4	5	4
Is applicable making conclusion and decision regarding the diagnostic / therapeutic approaches?	4	4	4	5	5	5	5	5	5	5
Demonstrates evidence of following a sequential analysis of the problem.	5	5	4	4	4	4	4	4	3	5
Self Directed Learning(Self study)			5				5	4	4	4
Defines learning objectives and learning goals.	5	4	5	5	5	5	5	5	4	4
Demonstrates evidence of accomplishment of learning objectives.	4	5	4	4	4	4	4	3	5	5
If necessary, seeks counseling to orient His/her study and willing to improve	5	4	5	5	5	5	4	5	4	5
Collaborative work							5	4	4	4
Works towards achievement of the groups learning goals with commitment.	5	4	5	4	3	5	4	4	4	5
Demonstrates effective interpersonal attributes.	4	5	4	5	5	4	5	5	5	4
Accepts feedback with openness.	3	5	5	4	4	5	5	5	5	5
Reacts positively to feedback and criticism.	4	3	5	4	4	4	4	4	4	5
Stands up for his/her points of view.	4	4	3	5	5	4	4	5	5	4
Shows ability to change his/her point of view of new information given/ obtained.	5	5	4	5	5	5	5	5	3	5

Signature of Facilitator

Pune District Education Association's
Seth Govind Raghunath Sable College of Pharmacy, Saswad

Feedback of students on PBL conducted on 03/12/2020

Subject: Pharmacology–II **Class:** Third Year B. Pharm.

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Do you think PBL is enhancing your comprehension and analytical skills?	✓		
Do you think PBL is enhancing your referencing & researching skills?	✓		
Do you think PBL is contributing towards improving your communication and presentation skills?	✓		
Do you think this activity should be continued in future also?	✓		

Suggestions if any,----------

----------Pl. tear from here before submitting----------

Name of the group leader..Peshave Tahaya..Signature.....T.A. Peshave....

Group No.: 41-50 (Group No-E)

Pune District Education Association's
Seth Govind Raghunath Sable College of Pharmacy, Saswad.

2020- 2021
PBL

Class: T. Y. B. Pharm. (Sem.-V)
Subject: Pharmacology-II
Date: 03/12/2020

Sr. No.	Facilitator's Name	Group	Roll number of the students
1.		A	1-10
2.		B	11-20
3.		C	21-30
4.		D	31-40
5.		E	41-50
6.		F	51-60
7.		G	61-67

Page No.
Date

Q.1 How does artial fibrillation differ from a normal heart rhythm?

→ Atrial fibrillation –

Atrial fibrillation (A-fib) is an irregular & often very rapid heart rhythm (arrhythmid) that can lead to blood clots in the heart. A-fib increases the risk of stroke heart failure & other heart related complication.

During atrial fibrillation, the heart upper chamber (the atria) beat choatically & irregularly - out of sync with the lower chambers of the heart. for many people, A-fib may have no symptoms However, A-fib cause a fast, pounding heartbeat shortness of breath or weakness.

Episodes of atrial fibrillation may come & go, or they may be persistent Although A-fib itself usually isn't lifethreatening, it's a serious medical condition that requires proper treatment to prevent strokes.

Treatment for atrial fibriallation may include medication, theapy to reset the heart rhythm & catheter procedure to block foulty heart signals.

A person with atrial fibrillation may also have a related heart rhythm problem called atrial flutter. Although atrial flutter is a different arythmia, the treatment is quite similar to atrial fibrillation.

Symptoms
- weakness
- shortness of breath

- sensation of the fast, fluttering or pounding heartbeat.
- chest pain
- Dizziness
- Fatigue
- lightheadedness
- Reduced ability to exercise

Cause

To understand the cause of a-fib it may be helful to know how the heart typically beats.

The typical heart has four chamber two upper chamber & two lower chamber. within the upper right chamber of the heart is a group of cells called sinus node.

In a regular heart rythm - The signal travels from the sinus node through the two upper heart chamber

The signal pases through a pathway bet^n the upper & the lower chamber called the atriventricular (AV) node. the movement of the signal cause your heart to squeeze (contract), sending blood to your heart & body

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Q.2. What is the purpose of the warfarin (coumadin in kakades case?

warfarin (brand name coumadin and Jantoven) is a prescribed medication used to pre-vent Harmful blood clots from forming or preve-ent or stop bleeding, but farmful blood clots can cause a stroke, heart attack deep vein thrombosis, or pulmonary embolism because warfarin interfers with the formalin of blood clots, it is called Anticoagulant's as "blood thinners" However warfarin does not thin the blood but instead causes the blood to take longer to form a clot.

The formation of a clot in the body is a complex process that inrolves multi-ple substances called the clotting factors Warfarin decreases the body's ability to form blood clots by blocking the formation of vitamin K is depending on the formation. the vitamin K is needed Therefore, by giving a medication that block the clotting factors, your body can stop harmful clots from forming and preven-ts clots from getting larger.

Kakade. A.N. has long standing history of an irregular heartbeat (atrial fibrillation) For irregular heartbeat for the which he takes the oral

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Anticoagulant warfarin (coumadin) Anticoagulant therapy prevents strokes and warf the most commonly used the vitamin K Antagonist (VKA) has been the standard Agents used to Reduce stroke risk in certa At patients with risk factors since 1950's

Historically, Warfarin has been the drug of choise, but it has often, bee underused due to it's narrow risk benef -t's interval and the need of frequent monitoring. It's being gradually eclipse by a variety of non vitamin K antagonist oral Anticoagulants (NOACs) that are demenstrating excellent safety and effecti -hess without the need for frequent mo -nitoring and subsequent dose Adjustment.

The Avaibility of several Pharmacological Approaches to anticoagulant as well as more through understand of risk factors for embolization & bleed -g has improved.

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Q. 3) What is PI/INR tell & and what are the expected levels for kakade & What is the purpose of the INR?

A prothrombin Time (PT) test measures how long it takes For a clots to Form in a Blood sample An INR (International Normalized Ratio) is a type of the calculation based on PI test results.

prothrombin is a Protein made by the liver. It is one of the saveral substances Know as clotting (coagulation) factors When you get a cut or other Injury that causes bleeding, your clotting factors work together to form a blood clots. clotting factors level that are two low can cause you to bleed too much after An Injury level that are too high can cause dangerous clot to form In your Arteries or veins

A PT/INR test helps find out If your blood is clotting normally, it also check to see if a medicine that prevent blood clots is working the way it should other Names - prothrombine time/ International normalized Ratio, PI

A PT/INR test is often done Alone With a partial prothrombine time pTT test A PTT test also cheaks For

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For clotting time.

The expected levels For kakade is INR range of 20 to 30.

IF you were tested because you are taking Warfarin. Will probably be in the Form of INR levels are often use because they make it easier to compare result from different labs & different t method, If you are not taking Warfarin, your Results may be in the for of IN levels of no. of second it takes for you blood sample to clot (prothrombin time)

If your are taking Warfarin -

= INR level that are too low may mean you a at risk for dangerous blood clots.

= INR levels that are two high may you mean are at risk for dangeroue bleeding.

Your heath care provider will Probably change your dose of warfarin to reduce these risks.

IF you are not taking Warfarin & your INR or prothrombine time Result were not normal, it may mean one or the following conditions.

- Liver Diseases.
- vitamin-K-Deficiency.
- A Bleeding or Clotting Disorder.

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Q.4. What happened when Kakade began taking the antibiotic?

Co-trimoxazole is a combination of two antibacterial bMedicines called sulfamethoxazole, & "trimethoprim". Although it has been prescribed widely for a range of infections in the past, it has very occassionally been associated with some serious side effects. As results, other antibiotics are now preffered to treat simple infections. In perticular, it is prescribed for Infections which can occur in people who have a problem with their immune systems. It works by killing the germs (bacteria) responsible for causing the Ifections.

Antibiotics can cause a no. of side effects. Nausea, diarhea, and allergic Reactions are some known side effects of Antibiotics. Antibiotics ~~are some known~~ also may kill naturally-occuring bacteria that protect the body, yeast infection, So yeast infections may occur while you are ~~taking~~ Antibiotics.

In some cases, it could happened within the 12 hrs of taking drug.

* Side effects of Antibiotics -

i) mild skin rasheh

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2) Allergic Reactions.

3) Loss of Apetite.

4) vaginal Infections.

5) short-term Diarrhea.

Antibiotics work by blocking vital process in bacteria, killing the bacteria or stopped them from multiplying. This hel the body's natural immune systems to figh the bacterial Infections. Antibiotics star working rights away after a persons take them. Each Antibiotics may stay in the body for different lengths of time but common Antibiotics such as Amoxicilin & Ciprofloxacin stay in your system for about 24 hrs after taking the last dose.

Once bacteria enter in your body your body's immune system tries fight them o but oftentimes, your body can't fight the Infections naturally, & you need of Antibiotics medication that kills the bacter

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Q.5) What should kakade have done to prevent this problem?

→ ① make healthy food choices.

② Watch your blood pressure

③ Quit smoking.

④ Get your cholesterol checked.

⑤ Get restful sleep.

① make healthy food choices -
For good health and disease prevention, Avoid ultra-progresed food and eat homemade meals prepared with the basic Ingredients.

Ultra processed food indwds -

① cookies
② chips
③ white bread
④ Donuts

② watch your blood pressure -
Do you have high blood pressure Even if you dont think so, keep focused. About 45% of Adults in the United states have hypertension defined as sytolic

blood pressure, diastolic blood pressure are taking medication of hypertension.

Normal blood pressure is defined As blood pressure < 120/80 mmHg. Having hypertension puts you at risk heart disease & stroke, which are leading causes of death in the United states.

③ Quit smoking -

The smokers lose at least 10 yrs of life expectancy compared with people never smoked. people who quit by age 40 reduced their risk of smoking-related by death 90%.

The smokers are more likely than nonsmokers to develoup heart disease different types of cancer stroke & more.

④ Get your cholesterol cheeked -

When cheeking your cholesterol, your test results will shows your cholesterol levels in miligrams per deciliters. It's crucial to get your cholesterol cheeked bcz your Doctor will be able to advices you on how maintane healthy levels, which turns lower chances of getting heart disease & stroke.

PAGE NO.:
DATE.

(5) Get Restful Sleep-

If you have trouble sleeping try to established a sleep routine. A good sleep routine inclwides going to a bed & walking up and athe same time every day. Avoiding ~~Heaving~~ eating heavy meals & alcohol. It's importanto to stop screen time from your devices 2 hrs befor -e bedtime, too.

To wind down before bed.

- Listen to calming music
- Read a book
- Practice 10 minutes of yoga

Pune District Education Association's
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2020- 2021

PBL -1 TRIGGER

Class: S. Y. B. Pharm. (Sem.-III) **Subject:** Pharmaceutical Organic Chemistry-II

Date: 24/03/2021 Platform: Online mode

An aromatic compound A on treatment with aqueous ammonia and heating forms compound B, which on heating with Br_2 and KOH forms a compound C of molecular formula C_6H_7N. Compound C gives Hinsberg test positive. It is also used as a intermediate in the synthesis of sulfa antibacterial drugs.

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Seth Govind Raghunath Sable College of Pharmacy, Saswad.

FACILITATOR's NOTES

Learning Objectives:

1) To learnt the inter conversion of organic compounds
2) To learn types of reactions.
3) To study reaction mechanism involved in synthesis of B and C.

Compilation of:

1) Write structures of compound A, B and C.
2) Write the equation for the reaction of compound A with aqueous ammonia.
3) Write the equation for conversion of compound B into compound C.
4) Explain the reaction mechanism of conversion of A into B.
5) Conversion of compound B to the compound C involves popular reaction. Give name and write in detail reaction mechanism of it.
6) Explain Hinsberg test.
7) Give examples of sulfa antibacterial drugs?

References:

1) Advanced Organic Chemistry by Bahl & Bahl, S Chand Publication, Twentieth Revised Edition, 2011.
2) Organic Chemistry by Morrison & Boyd, 6th edition, Pearson Education.
3) Advanced General Organic Chemistry A Modern Approach by S. K. Ghosh, New Central Book Agency (P) Ltd.,3rd edition.

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2020- 2021
PBL

Class: S. Y. B. Pharm. (Sem.-III))
Subject: Pharmaceutical Organic Chemistry-II
Date: 24/03/2021
Platform: Online mode

Sr. No.	Facilitator's Name	Group	Roll number of the students	Name of group leader
1.	Prof. J. R. Jagtap	A	1-10	Beldar Prajakta Mahesh
2.		B	11-20	Gaikwad Shruti Surendra
3.		C	21-30	Kawade Anagha Avinash
4.		D	31-40	Kunjir Kalyani Suresh
5.		E	41-50	Patil Manasi Satish
6.		F	51-60	Wagh Poonam Gorakhnath
7.		G	61-70	Zende Prasad Ramesh

Name and sign of facilitator
(Mrs. J. R. Jagtap)

Pune District Education Association's
Seth GovindRaghunath Sable College of Pharmacy, Saswad

PBL -1

Class: S. Y. B. Pharm. (Sem.-III) **Subject:** Pharmaceutical Organic Chemistry-II

Date: 24/03/2021

Attendance Sheet

Roll No.	Group No.	Name of Students	Attendance
1	A	Beldar Prajakta Mahesh	P
2		Bhorade Dipti Sham	P
3		Bhosale Tanuja Rahul	P
4		Chandgude Kshitija Laxman	P
5		Deshmukh Avishkar Vijay	P
6		Devi Archana	P
7		Dhage Vikas Baburao	P
8		Dhavale Sahil	A
9		Dhole Isha Popat	P
10		Dodke Chetana Ashok	P
11	B	Dorge Akash Abaso	P
12		Gaikwad Sakshi Rajendra	P
13		Gaikwad Shruti Surendra	P
14		Gaikwad Sujit Dnyandev	P
15		Gawade Omkar Vijay	P
16		Gore Abhijeet Vitthal	P
17		Jadhao Anil Ganesh	P
18		Jadhav Adesh Vijaykumar	P
19		Jadhav Shivani Ramesh	P
20		Jadhavswarup Brijesh	P
21	C	Jadhav Vaishanvi Shivaji	P
22		Jagtap Sahil Sunil	P
23		Javalkar Aditya Hanumant	P
24		Kale Sakshi Ravindra	P
25		Kande Tanuja Kondiba	P
26		Kawade Anagha Avinash	P
27		Khaire Mayuri Sunil	P
28		Khaire Yogita Shailesh	P
29		Khaladkar Ruta Vinayak	P
30		Kharat Akash Bhagwanrao	P

31	D	Khedekar Raj Ashok	P
32		Kondhalkar Omkar Balaso	P
33		Kulkarni Omkar Sanjay	P
34		Kunjir Kalyani Suresh	P
35		Mahala Ruchita Ramesh	P
36		Marewar Swati Surakant	P
37		Mundlik Pratham Santosh	P
38		Natu Chetan Mohan	P
39		Nikate Shrinivas Kishor	P
40		Nimbalkar Yash Gorakh	P
41	E	Padher Achal Dattatray	P
42		Pandit Prateeksha Dnyandeo	P
43		Parsalge Mahadev Shyam	P
44		Patil Manasi Satish	P
45		Pawar Aditya Ashok	P
46		Raut Ashish Umesh	P
47		Rokade Vishalakshi Sanjay	P
48		Salunkhe Dhanashri Sanjay	P
49		Sarwaderanjeet	A
50		Sathe Om Vilas	P
51	F	Shiekh Farhan Nazir	P
52		Shipalkar Kalyani Hanumant	P
53		Shitole Shreya Raju	P
54		Takawale Omkar Ramesh	P
55		Tanpure Harshad Nagesh	P
56		Taware Chetana Rajkumar	A
57		Wagh Poonam Gorakhnath	P
58		Yadav Abhishek Mahadev	P
59		Yadav Anchal Dadaso	P
60		Zagade Ritusha Rajendra	P
61	G	Zende Prasad Ramesh	P
62		Zende Priyanka Jalindar	P
63		Darade Gitanjali	P
64		Kshirsagar Vaishnavi	P
65		Lohokare Chaitali	P
66		Bhilare Sejal Anil	P
67		Darekar Akash Madhukar	P
68		Darkonde Nikhil Ravindra	P
69		Gade Samadhan Ganpat	P
70		Jagtap Chaitali Hemraj	P

Name and Sign of Facilitator
(Mrs. J. R. Jagtap)

Pune District Education Association's
Seth Govind Raghunath Sable College of Pharmacy, Saswad.

2020- 2021

Class: S. Y. B. Pharm. (Sem.-III) **Subject**: Pharmaceutical Organic Chemistry-II
Group No- 4

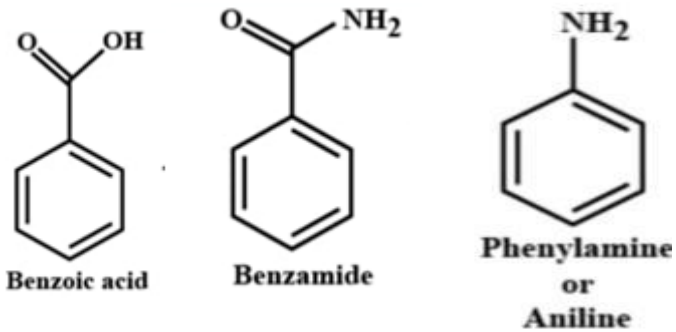
Attendance

Roll No.	Name of Students	Email	Attendance
31	Khedekar Raj Ashok	rajkhedekar215121@gmail.com	Present
32	Kondhalkar Omkar Balaso	omkarkondhalkar0218@gmail.com	Present
33	Kulkarni Omkar Sanjay	omkarkulkarni646@gmail.com	Present
34	Kunjir Kalyani Suresh	kalyanikunjir5924@gmail.com	Present
35	Mahala Ruchita Ramesh	mahalaruchi2000@gmail.com	Present
36	Marewar Swati Surakant	ssm19121999@gmail.com	Present
37	Mundlik Pratham Santosh	mundlikpratham@gmail.com	Present
38	Natu Chetan Mohan	natuchetan@gmail.com	Present
39	Nikate Shrinivas Kishor	shrinivasnikate@gmail.com	Present
40	Nimbalkar Yash Gorakh	ynimbalkar2612@gmail.com	Present

.

Solutions

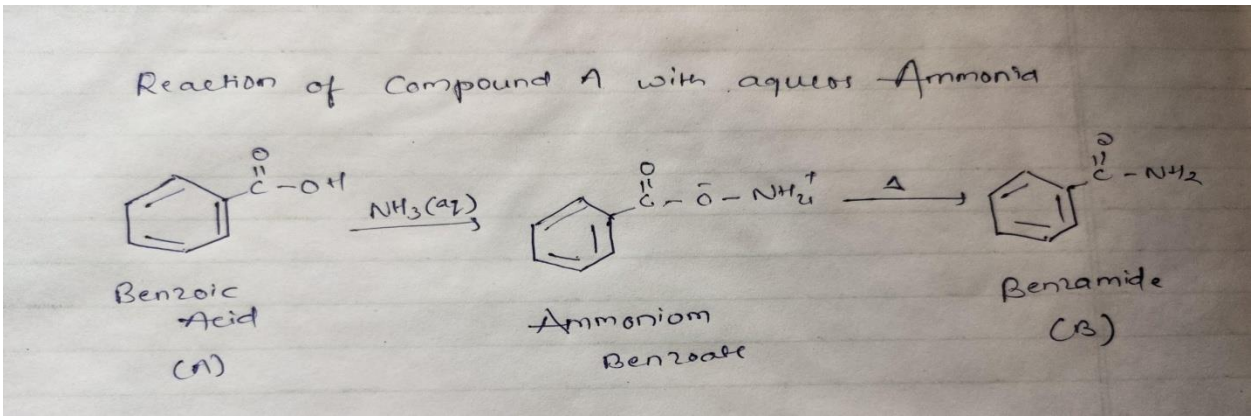
1.Write structures of compound A,B and C.
Ans:



(A) **(B).** **(C)**

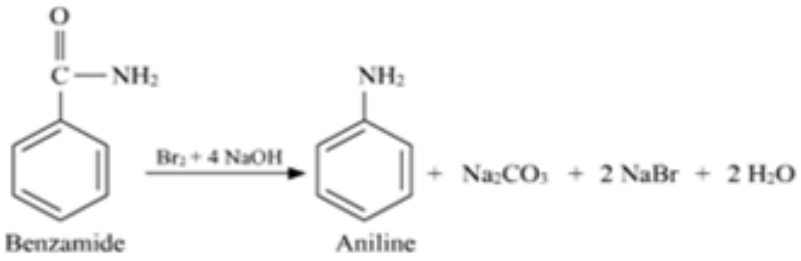
2.Write the equation for the reaction of compound A with aqueous ammonia.
Ans.

- **Benzoic Acid r**eacts with **[aq] ammonia** to give **ammonium benzoate** and further on heating it gives **Benzamide**

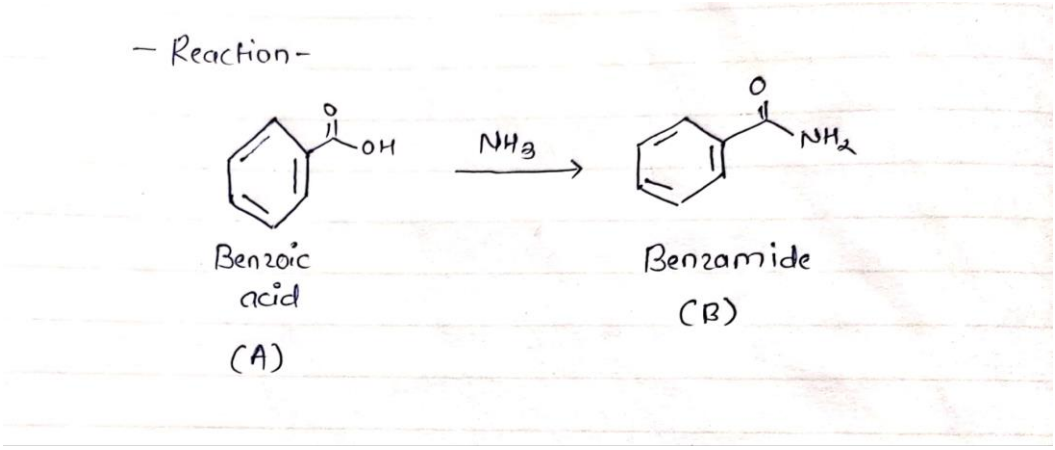


3.Write the equation for conversion of compound B into compound C.
Ans.

Benzamide on heating with a mixture of Br2 in presence of NaOH or KOH (i.e. NaOBr or KOBr) is given aniline.



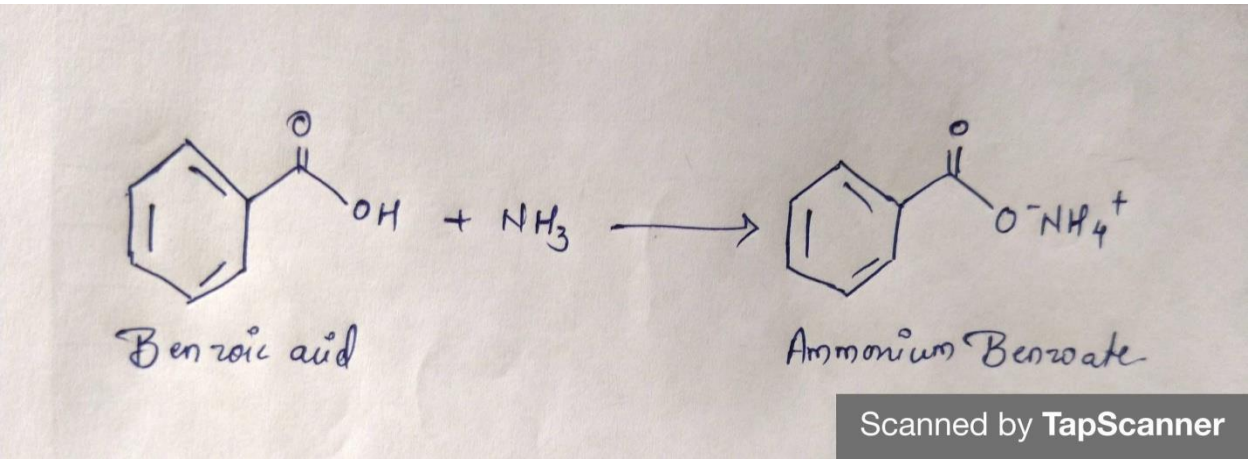
4.Explain the reaction mechanism of conversion of A into B.
Ans-Benzoic acid reacts with Ammonia gives Benzamide.
Reaction:-



Reaction mechanism-

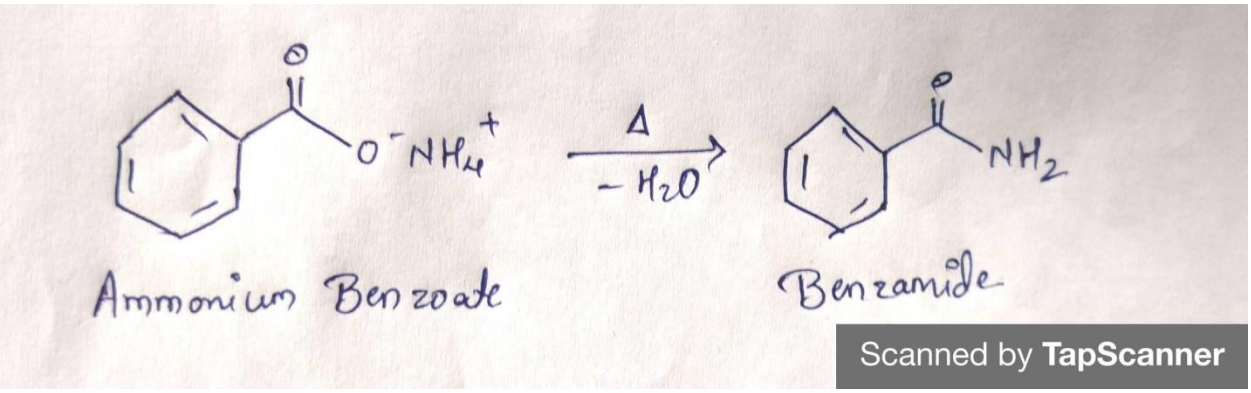
Step-1:

Benzoic acid reacts with aqueous ammonia to give ammonium benzoate which is salt of ammonia.

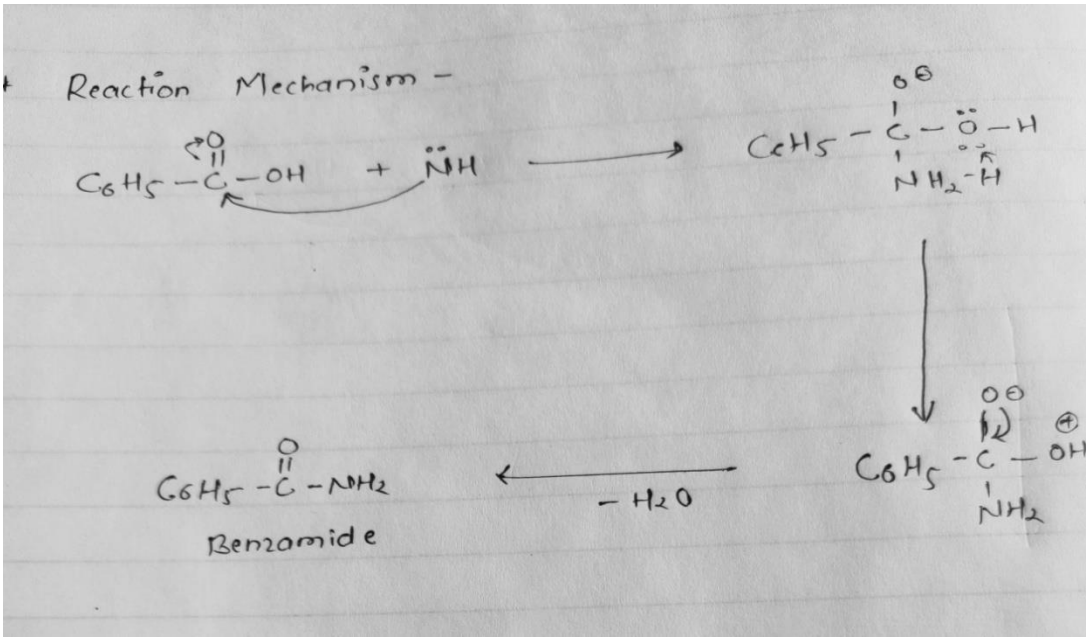


Step-2:

Ammonium benzoate on heating loses a molecule of water to form Benzamide.



Reaction mechanism :-



5.Conversion of compound B to the compound C involves popular reaction. Give name and write in detail reaction.

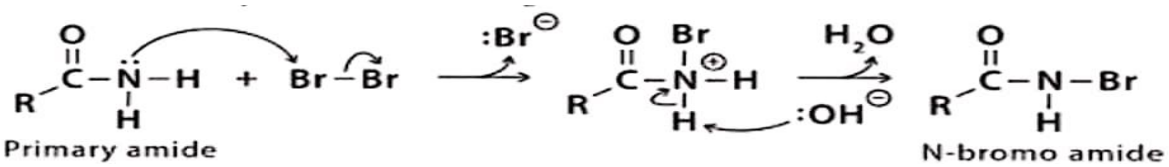
Ans:-

a) Name:- Hoffman degradation reaction

- **The Hofmann rearrangement** (Hofmann degradation) is the organic reaction of a primary amide to a primary amine with one fewer carbon atom. The reaction involves oxidation of the nitrogen followed by rearrangement of the carbonyl and nitrogen to give an isocyanate intermediate.

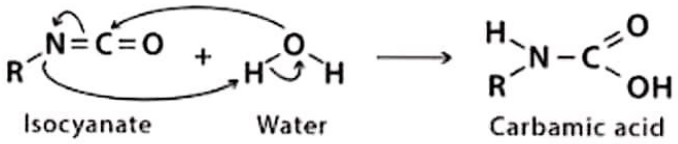
Mechanism of Hoffman Rearrangement

Step 1:- Breakage of N-H and the formation of N-Br in the presence of sodium hydroxide ttresulting in n-bromo amide

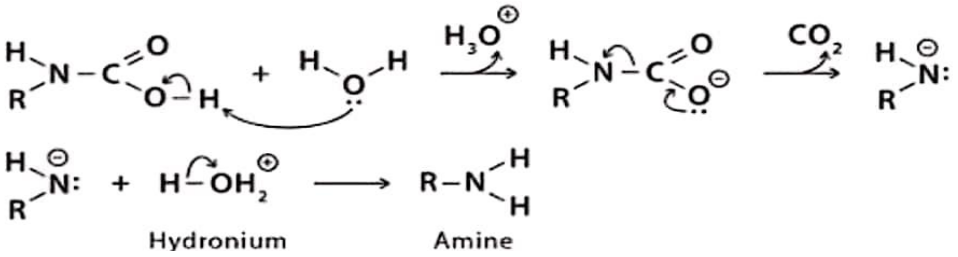


Step 2:- Migration of a carbon atom to displace the bromide group on adjacent nitrogen followed by deprotonation of the N-H bond giving a neutral isocyanate

Step 3:- Attack on the iso cyanate by water followed by proton transfer resutlting in an unstable carbamic acid



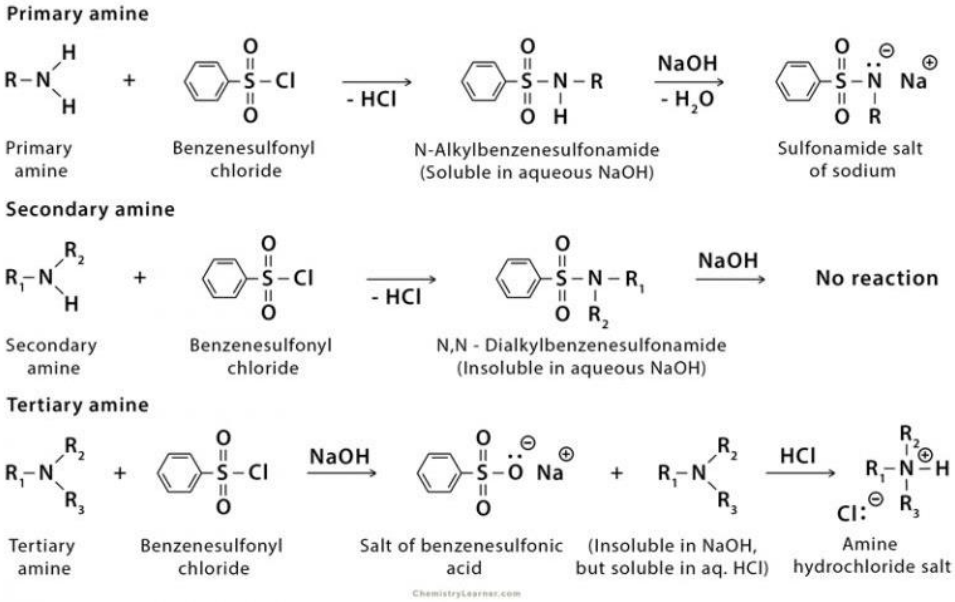
Step 4 :- Thermal degradation of the carbamic acid releasing carbon dioxide gas resulting in an amine after protonation



6.Explain Hinsberg test.

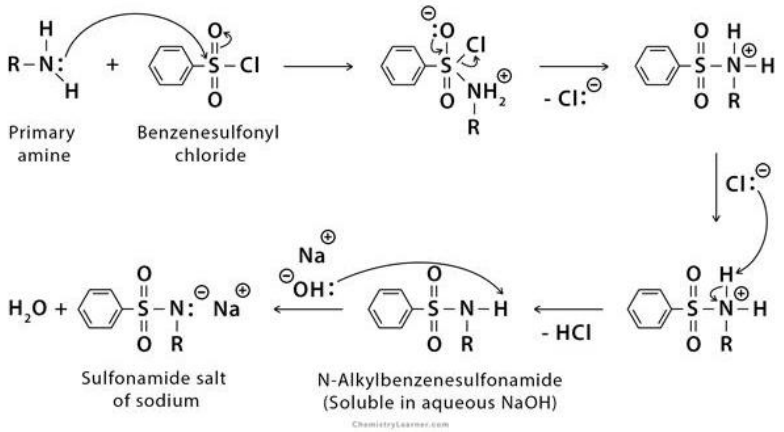
Ans.

Hinsberg test is a chemical reaction that can distinguish between primary, secondary, tertiary amines. The amine is shaken well with Hinsberg reagent in the presence of aqueous alkali (e.g., KOH or NaOH).



Mechanism of Hinsberg Test

The amine first reacts with benzenesulfonyl chloride in an addition-elimination reaction on the highly electrophilic sulfonyl chloride derivative. After the stepwise loss of the chlorine and one proton from the amine in the presence of sodium hydroxide, the resulting product is a sulfonamide salt of sodium.

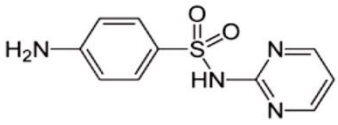


7.Give examples of Sulfa Antibacterial Drugs?

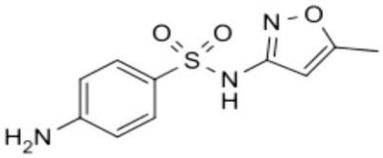
Ans. <u>Definition</u> :- Sulfa drugs were the first chemical substances systematically used to treat and prevent bacterial infections in humans. Their use has diminished because of the availability of antibiotics that are more effective and safer and because of increased instances of drug resistance.

-Structures:-

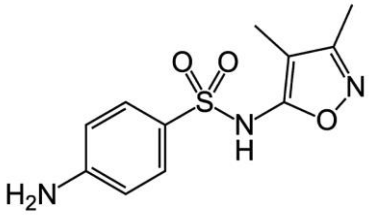
1) **<u>Sulfadiazine :-</u>**



2) **Sulfamethoxazole :-**



3) **Sulfisoxazole :-**



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Feedback of students on PBL conducted on 24/03/2021
Subject: Pharmaceutical Organic Chemistry-II Class: S. Y. B. Pharm. (Sem.-III)

- **This questionnaire has been designed to understand the opinion of students involved in the PBL activity so that the activity can be improved in the future. The group leader is advised to answer the questions on behalf of all the group members.**

Please tick the appropriate box: Please **tick** the appropriate box:

Trigger	Yes	No	Can't say
Was the trigger provided to you easily understandable?	√		
Was the trigger interesting?	√		
Could you relate the trigger to your curriculum?	√		
Role of facilitator	√		
Did you find the role of facilitator useful in understanding the problem?	√		
Did you take the help of the facilitator in identifying the objectives of the problem?	√		
Resources	√		
Did you refer to the books available in the library for compiling the data related to your problem?	√		
Were there sufficient reference books available in the library for researching the problem?	√		
Did you find the internet facility and online resources adequate?	√		
Overall activity	√		
Do you think PBL is enhancing your comprehension and analytical skills?	√		
Do you think PBL is enhancing your referencing & researching skills?	√		
Do you think PBL is contributing towards improving your communication and presentation skills?	√		
Do you think this activity should be continued in future also?	√		

Suggestions if any,----------

----------Pl. tear from here before submitting----------

Name of the group leader: Kalyani Suresh Kunjir Signature…….
Group No.: 4

Pune District Education Association's

Seth Govind Raghunath Sable College of Pharmacy, Saswad.

FACILITATOR ASSESSMENT FORM

PBL No.: 1 Date: 24/03/2021

Subject: Pharmaceutical Organic Chemistry-II Cass: S. Y. B. Pharm. (Sem.-III)

Please rate in the 5 point scale: 5- Excellent, 4- Very Good, 3- Good, 2- Satisfactory, 1 - Not satisfactory

Roll No. of the student / **Criteria**	31	32	33	34	35	36	37	38	39	40
Application of knowledge base										
Applies previous knowledge to clarify and define the problem.	3	4	2	4	3	3	2	5	5	3
Answers questions and shares his/her opinions by applying acquired knowledge.	3	4	2	4	3	3	2	5	5	3
Critical Thinking										
Demonstrate, evidence, critical understanding and critical analysis facts.	3	4	2	4	3	3	2	5	5	3
Is applicable making conclusion and decision regarding the diagnostic / therapeutic approaches?	3	4	2	4	3	3	2	5	5	3
Demonstrates evidence of following a sequential analysis of the problem.	3	4	2	4	3	3	2	5	5	3
Self Directed Learning(Self study)										
Defines learning objectives and learning goals.	3	4	2	4	3	3	2	5	5	3
Demonstrates evidence of accomplishment of learning objectives.	3	4	2	4	3	3	2	5	5	3
If necessary, seeks counseling to orient His/her study and willing to improve	3	4	2	4	3	3	2	5	5	3
Collaborative work										
Works towards achievement of the groups learning goals with commitment.	3	4	2	4	3	3	2	5	5	3
Demonstrates effective interpersonal attributes.	3	4	2	4	3	3	2	5	5	3
Accepts feedback with openness.	3	4	2	4	3	3	2	5	5	3
Reacts positively to feedback and criticism.	3	4	2	4	3	3	2	5	5	3
Stands up for his/her points of view.	3	4	2	4	3	3	2	5	5	3
Shows ability to change his/her point of view of new information given/ obtained.	3	4	2	4	3	3	2	5	5	3

Signature of Facilitator

Pune District Education Association's
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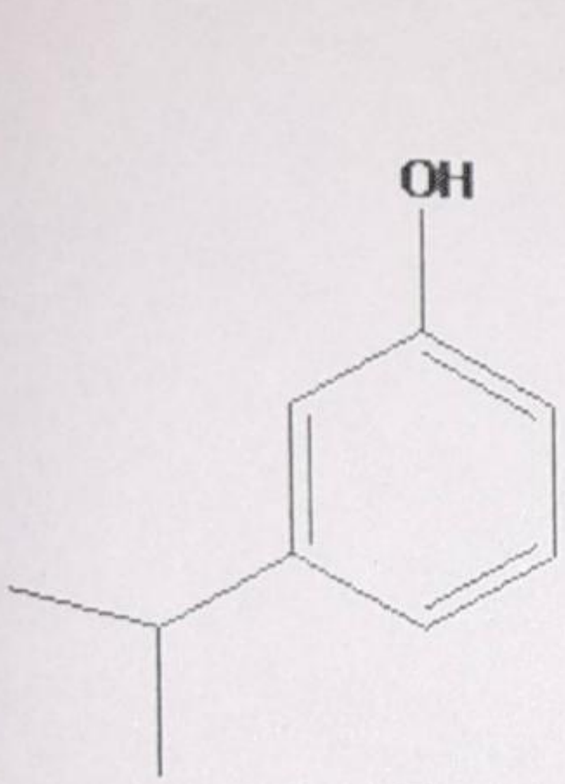
2020- 2021

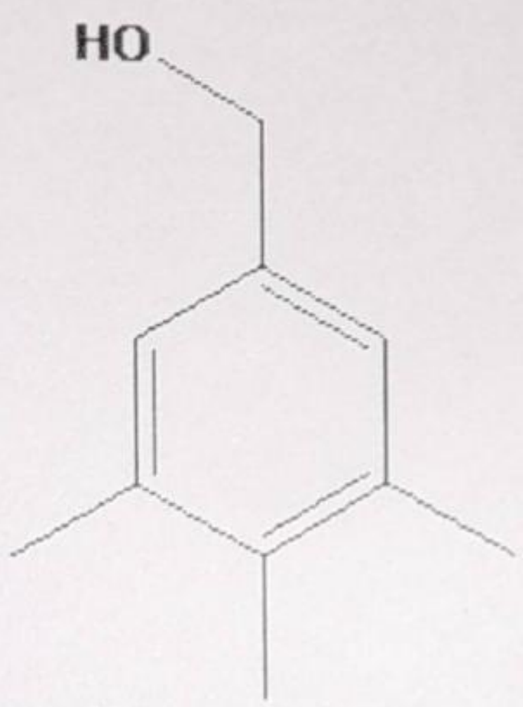
PBL -1 TRIGGER

Class: F. Y. B. Pharm. (Sem.-II) **Subject:** Pharmaceutical Organic Chemistry-I

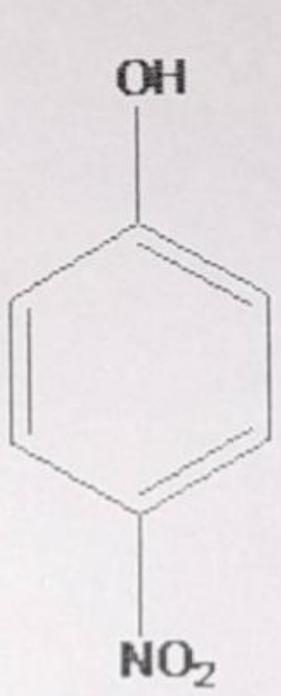
Date: 30/07/2021



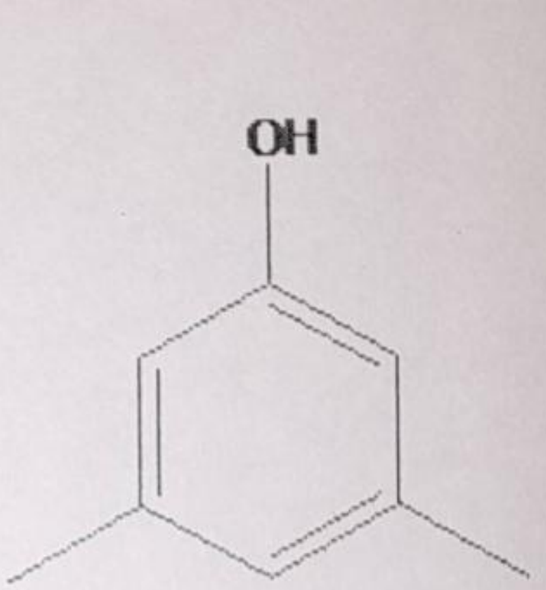
I



II



III



IV

III<IV<I<II

I<III<IV<II

II<I<IV<III

I<II<IV<III

Arrange the above compounds in order of increasing acidity (least acidic first)

Pune District Education Association's

Seth Govind Raghunath Sable College of Pharmacy, Saswad.

FACILITATOR's NOTES

Learning Objectives:

1) To learnt about acidity of organic compounds
2) To learnt about the different functional groups and its acidity
3) To study effect of substituent on acidity of organic compounds.

Compilation of:

1) Select correct option of acidity order.
2) Give explanation of correct option
3) Give explanation of incorrect options
4) Explain about acidity of organic compounds.
5) Explain effect of substituent on acidity of organic compounds.

References:

1) Advanced Organic Chemistry by Bahl & Bahl, S Chand Publication, Twentieth Revised Edition, 2011.
2) Organic Chemistry by Morrison & Boyd, 6th edition, Pearson Education.
3) Advanced General Organic Chemistry A Modern Approach by S. K. Ghosh, New Central Book Agency (P) Ltd.,3rd edition.

Group - 03 (21 - 30)

Page No.
Date / /

Pune District Education Association's
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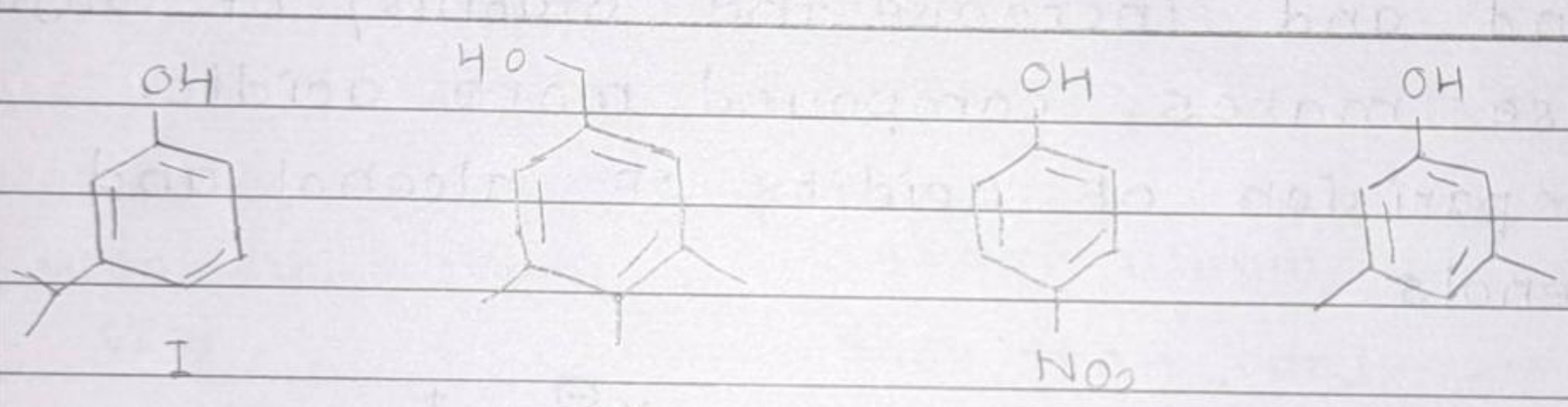
Pharmacy, saswad.

PBL - 1 Trigger.

class - F.Y. B.Pharm (sem. II)
Subject - Pharmaceutical Organic Chemistry - I.
Date - 30/07/2021.



I II I < IV < I < II

I < III < IV < II

II < I < IV < III

I < II < IV < III

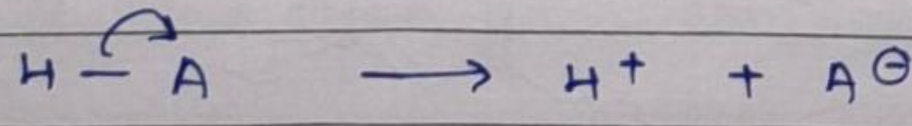
Arrange the above compounds in order of increasing acidity (least acidic first).

Answer - option-3.

Explanation -

The acids which can donate proton on ionization.

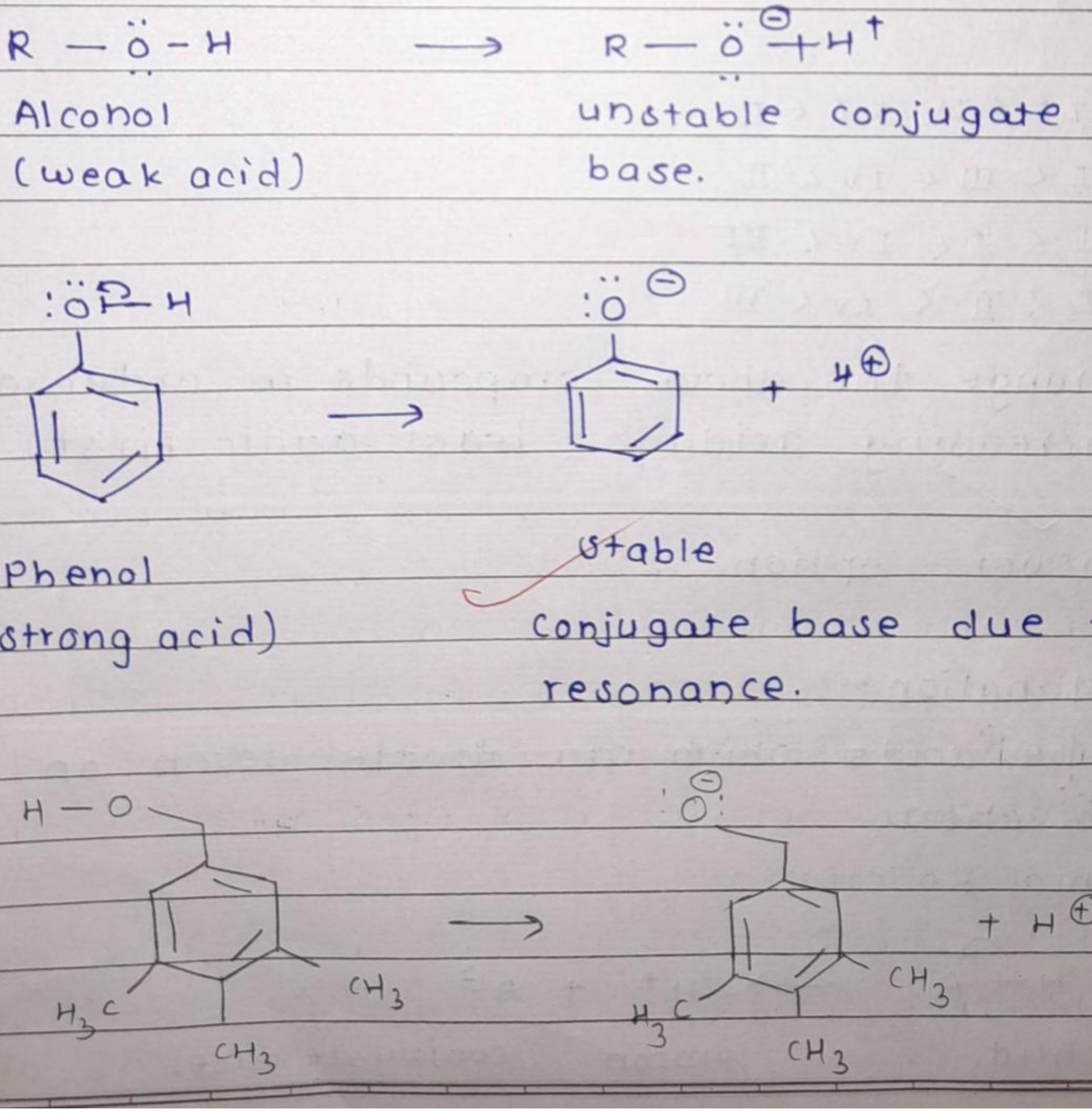
Genral Reaction -



Acid proton conjugate base.

The acidity of compound depends on bond strength of H-A. For to ionize it is essential to break the bond between H-A When H-A bond is weak the acid is strongest vice-versa. Also acids on ionization gives proton and conjugate base. It stability of conjugate base is high the corresponding acid is strong. so the neighbouring group is weaker H-A bond and increase the stability of conjugate base makes compound more acidic.

comparision of acidity of alcohol and phenols.

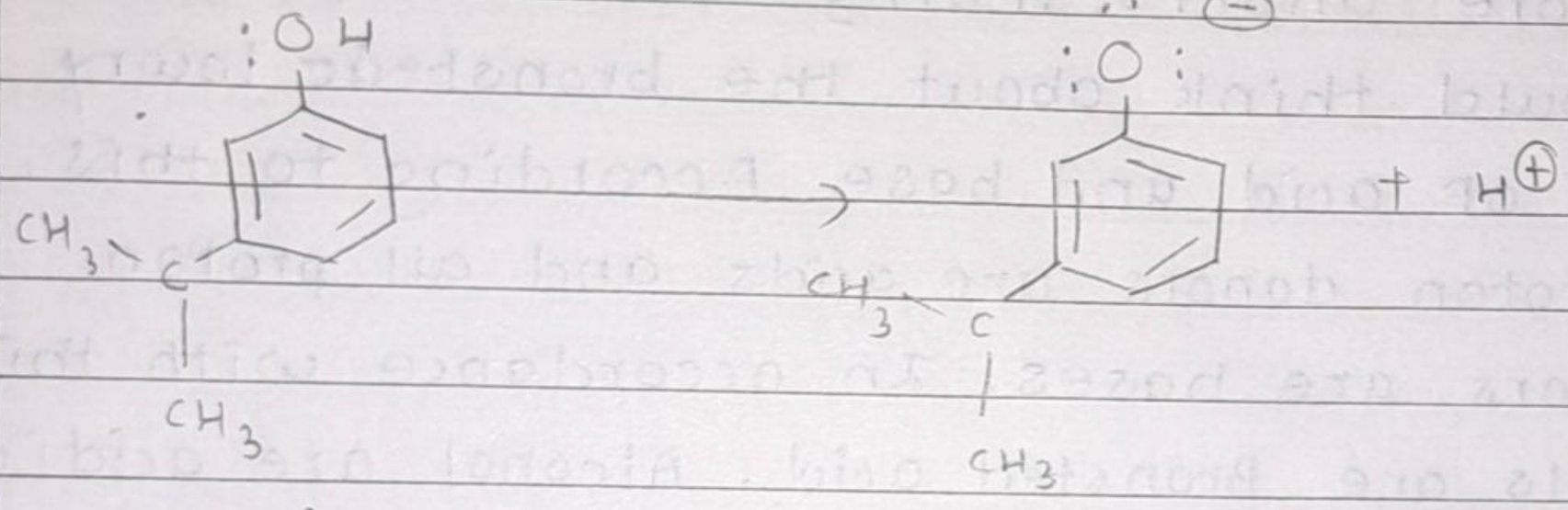


(II)

Alcohol (weak acid than phenols)

least stable (very unstable)

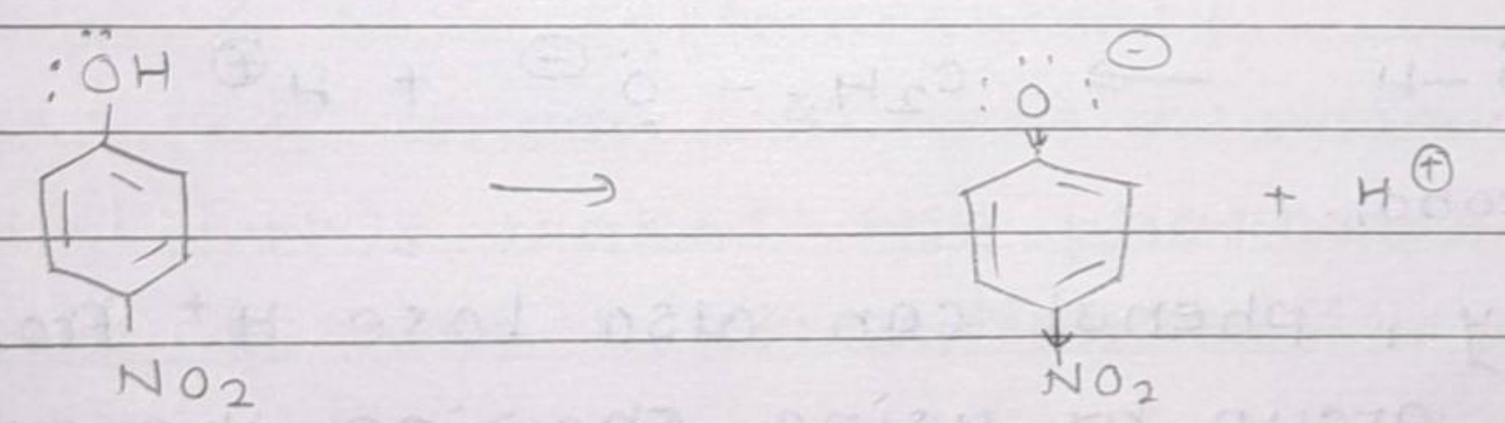
3, 4, 5 trimethyl benzyl alcohol.



(I)

weak acid than (IV)

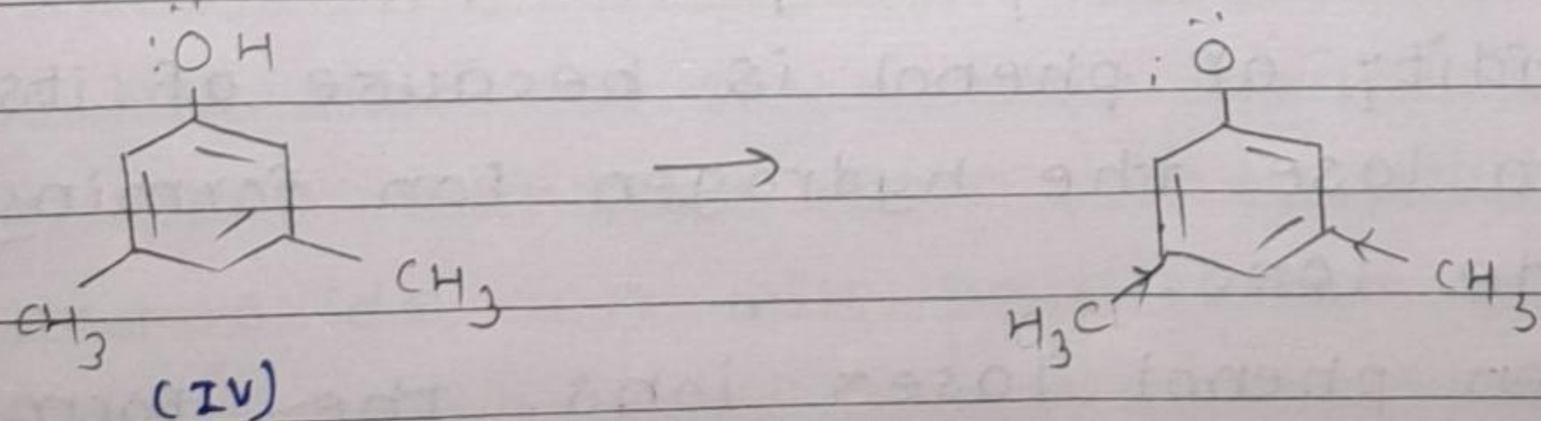
least stable conjugate base than conjugate base of III & IV due e⊖ donating group ($-CH(CH_3)_2$)



(III)

strong acid

Most stable conjugate base due to $e^{\ominus}$ withdrawing NO_2 group.



(IV)

weak acid than (III)

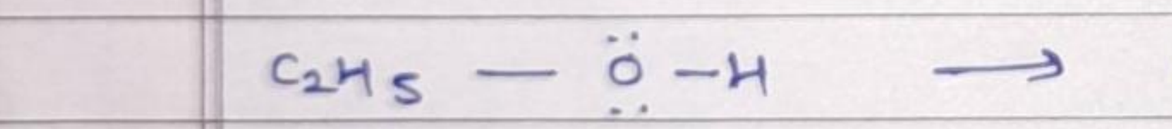
conjugate base least stable than conjugate base of III due to presence of $e^{\ominus}$ donating group

Therefore the compounds with increasing acidity order are

II < I < IV < III

Que-1 What is the acidity of alcohols?

Before understanding the acidity of alcohols, we should think about the bronstede lowry concept of acid and base. According to this, all proton donors are acids and all proton acceptors are bases. In accordance with this, alcohols are Bronsted acid. Alcohol are acidic due to polarity of the O-H bond. Owing to this, the shared pair of electrons shifts towards the O atom, and the O-H bond becomes weak. This facilitates the release of a proton them from the alcohol molecule making them acidic.



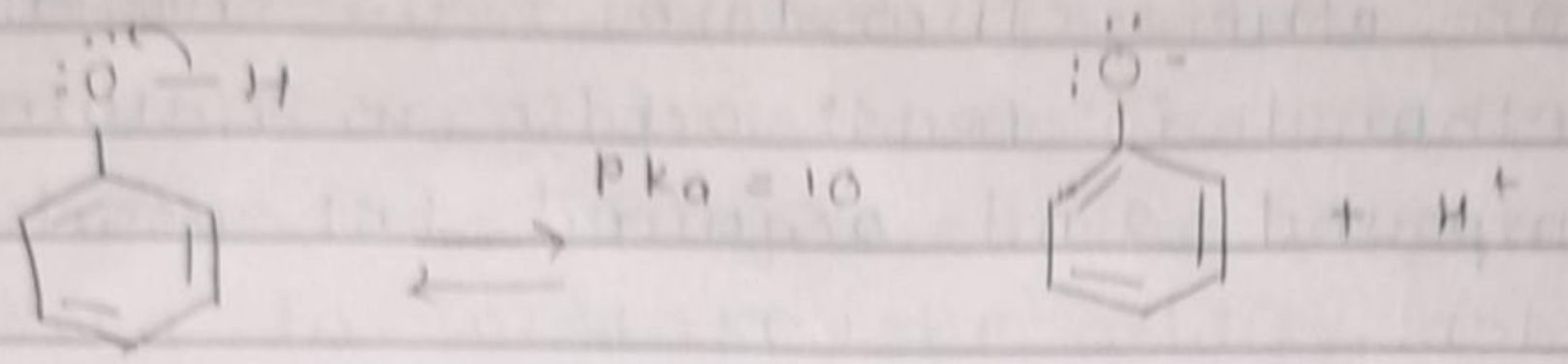
Ethyl alcohol.

Similarly, phenol can also lose H^+ from the -OH group by using showing the acidic behaviour.

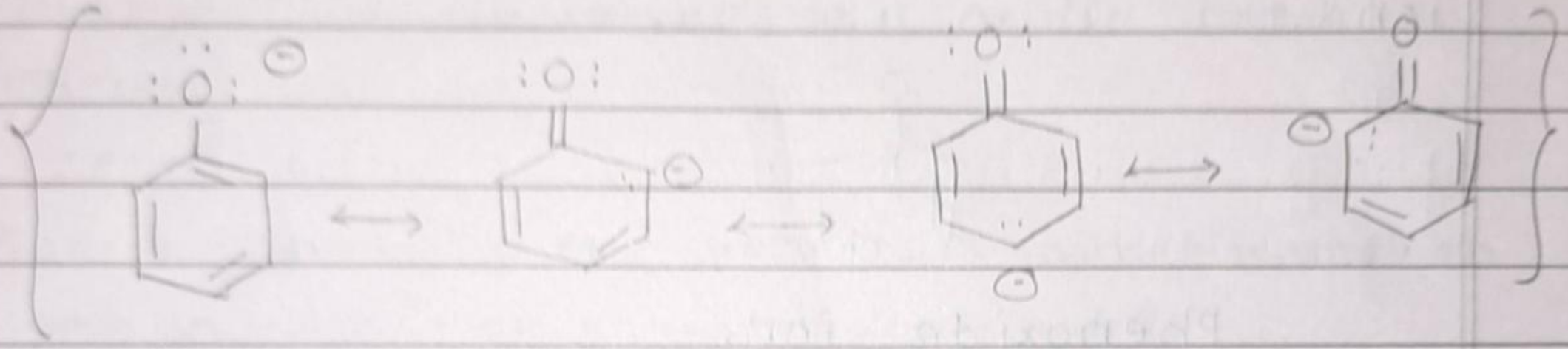
What is the acidity of phenol?

The acidity of phenol is because of its ability to lose the hydrogen ion forming phenoxide ions.

When phenol loses ions, they form a phenoxide ion.



The phenoxide structure forms as,



This phenoxide ion structure has a few special properties that are :

Phenoxide ion is well established due to the resonance.

The oxygen is connected to sp^2 carbon, which has a high electronegativity.

So, the carbon will pull e^- from the oxygen.

And, this makes the phenoxide ion stable due to the distribution of the electronegativity charge.

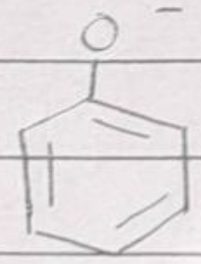
Since, the phenoxide ion is completly stable, phenol readily loses a hydrogen ion and shows the acidic character.

However, if any substituent is attached to the benzene ring, the stability of the phenoxide ion will be affected.

Due absence of resonance stabilizing compound alcohol compounds are less acidic than phenol compound i.e. compound 2nd will be less acidic

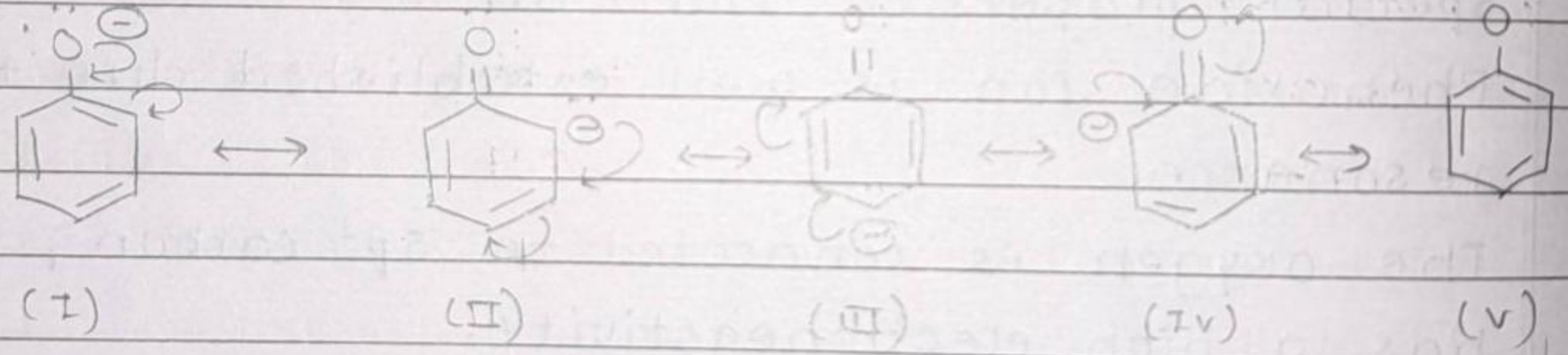
than others. Therefore 3,4,5-trimethylphenyl) methanol is least acidic in nature. So compound 2nd acquired 1st position in order.

Write the resonating structure of phenoxide ions.



Phenoxide ion.

Resonating structure of phenoxide ion :



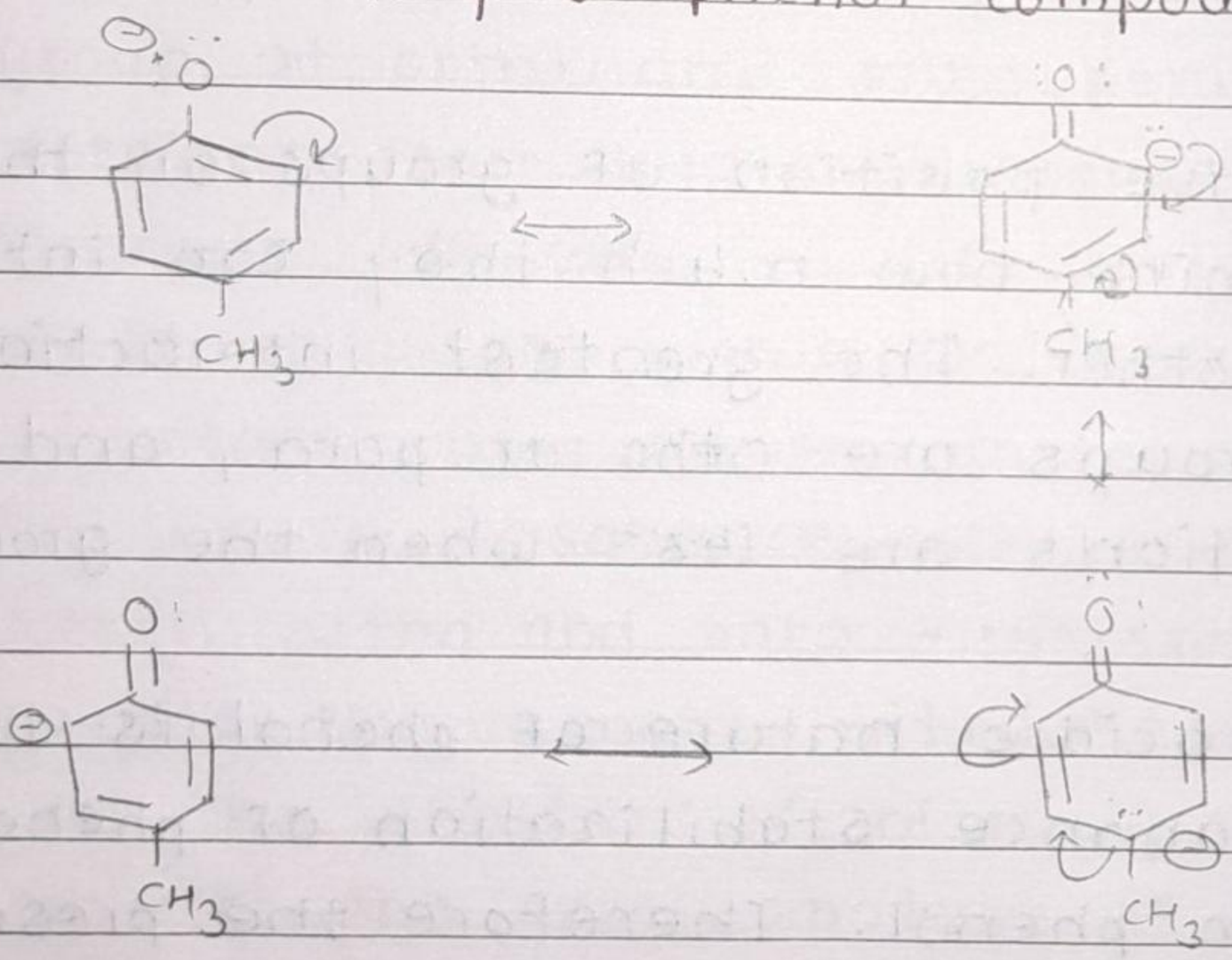
Phenoxide ion has the molecular formula C_6H_5O and its molecular weight is 93.1 g/mol Phenoxide ions contains non-equivalent resonance structures in which negatively charge is there which is less effectively delocalised over less electronegative carbon atom and one oxygen atom.

Que-3 Why phenol is more acidic than alcohol ?

As the acidic nature of phenol is due to the resonance stabilization of phenate

compared to ~~phe~~ alcohol. Therefore the presence of any substituent on aromatic ring which can stabilized the phenoxide ion will tend to increase the acidity of phenol. while any substituent which destabilized the phenate ion by increasing the negative charge will decrease the acidic nature of phenol.

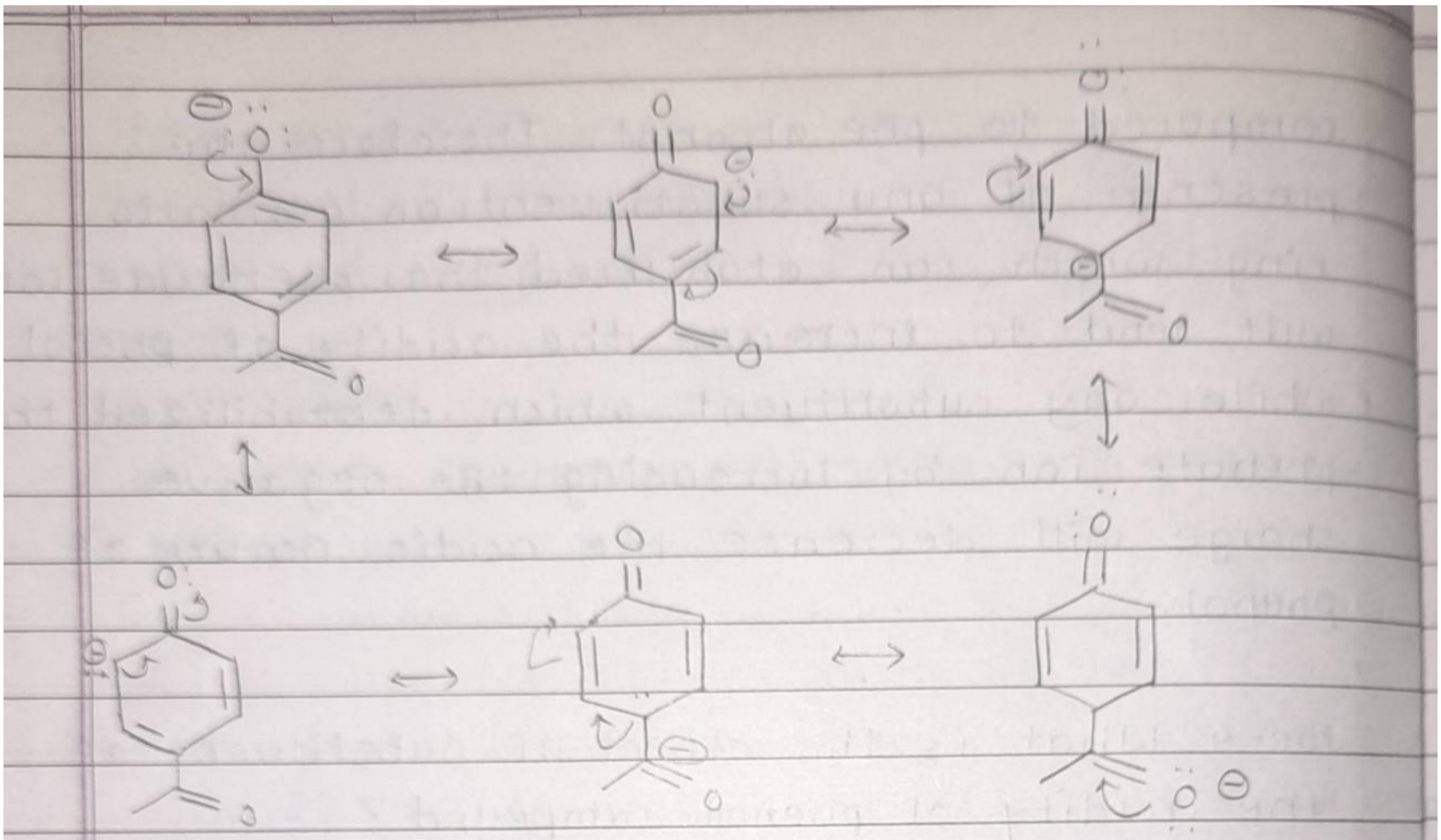
Que-4 What is the effect of substituent on the acidity of phenol compound?



Negative charge next to an electron donor is bad.

The effect of electron donating groups on a phenol is to make it less acidic. for example consider the resonance structure for the following phenoxide:

However, if an electron withdrawing group on the ring can further delocalise the negative charges than anion is more stable and the phenol is more acidic.



The relative position of groups on the ring determine how much they can interact with each other. The greatest interaction is when groups are otho or para, and the interactions are less when the group is meta.

As the acidic nature of phenol is due to the resonance stabilization of phenate compared to phenol. Therefore the presence of any substituent on the aromatic ring which can stabilize the phenoxide ion will tend to increase the acidity of phenol. While any substituent which destabilized the phenol.

Ion by increasing the negative charge will decrease the acidic nature of phenol. In other words: the presence of an electron withdrawing group on a benzene ring in

phenol increases the acidity of phenol & electron releasing group will decreases the acidity. for example, it there is nitro group substituent on phenol it will increases the acidity of phenol. Hence nitrophenol will be more acidic than phenol. as the nitro group imparts negative mesomeric effect and negative inductive effect. Hence, acts as electron withdrawing group.

The position of nitro group on the phenol will affects the acidity of phenol. A nitro group at ortho and para position withdraw electron from hydroxyl group of phenol by stronger -M effect while nitro group at meta position withdraws electron by weaker -I effect only as the meta position cannot involve in resonance with hydroxyl group. Hence ortho and para - nitrophenol are more acidic than meta - nitrophenol. similarly, as the number of nitro group increase on phenol the acidic nature of phenol increases.

Que-5 What is electron donating group and explain their effect on acidity of phenol compound.

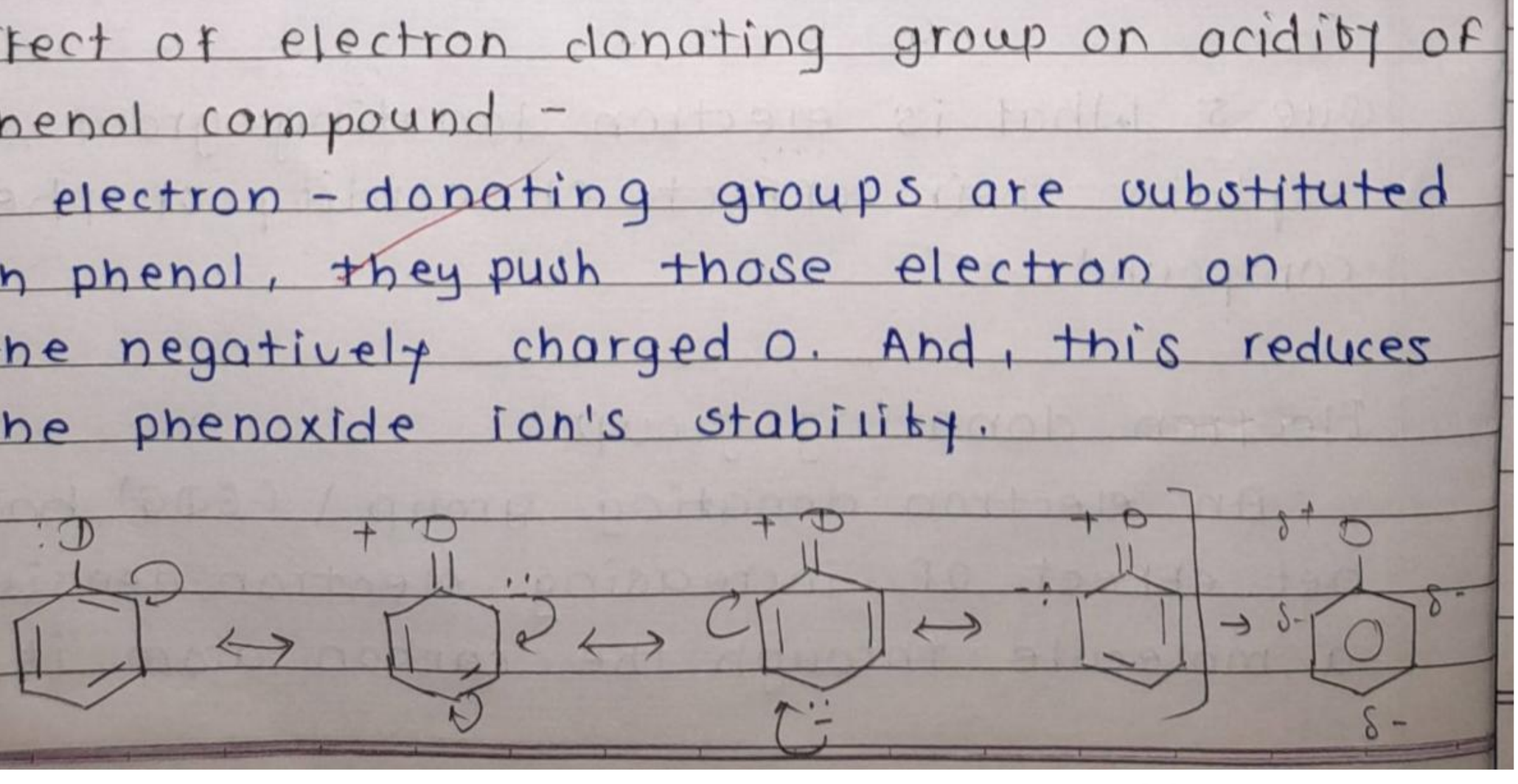
Electron donating group -

An electron donating group \ (EDG) has the net effect of increasing electron density in a molecule through the carbon atom it is

bonded to. By increasing electron density on adjacent carbon atoms, EDGs change the reactivity of a molecule:
EDGs make nucleophile stronger. with EDGs attached, a nucleophile centre is even more electron rich and ready to attack electrophile sites.
EDGs make carbon centers, weaker electrophi and less reactive to nucleophiles, because any (partial) positive charge it has will be minimized or nullified if the EDG is strong enough. Examples of good electron donating groups are groups with loan pairs to donate, such as:
The oxygen anion $-O^-$
Alcohol groups $-OH$
Amine groups $-NH_2$ or $-NR_2$.
Ethers $-OR$.
Alkyl groups are also weakly electron-donating.

Effect of electron donating group on acidity of phenol compound -

electron-donating groups are substituted on phenol, they push those electron on the negatively charged O. And, this reduces the phenoxide ion's stability.



So, if the electron-donating groups are substituted on phenol, resultantly, its acidity reduces. Due to this reason, cresol is less acidic than phenol.

From the above conclusion compound IV acquired 3 position in order and compound I st acquired 2nd positions in order.

Que-6 What is electron withdrawing group and explain their effect on acidity of phenol compound?

Electron withdrawing group -

An electron withdrawing group / (EWG) is a group that reduces electron density in a adjacent carbon atoms, EWGs change the reactivity of a molecule:

EWGs make electrophile stronger, because the electron-withdrawing effect makes any carbon centre even more electron deficient than before. EWGs make any nucleophile species less reactive, for the same reason as they strengthen electrophile Nucleophiles need electron density to react with electrophile:, if an EWG is 'withdrawing' electrons, this taking away the source of the nucleophile's strength.

The strongest EWGs are groups with pi bonds to electronegative atoms:

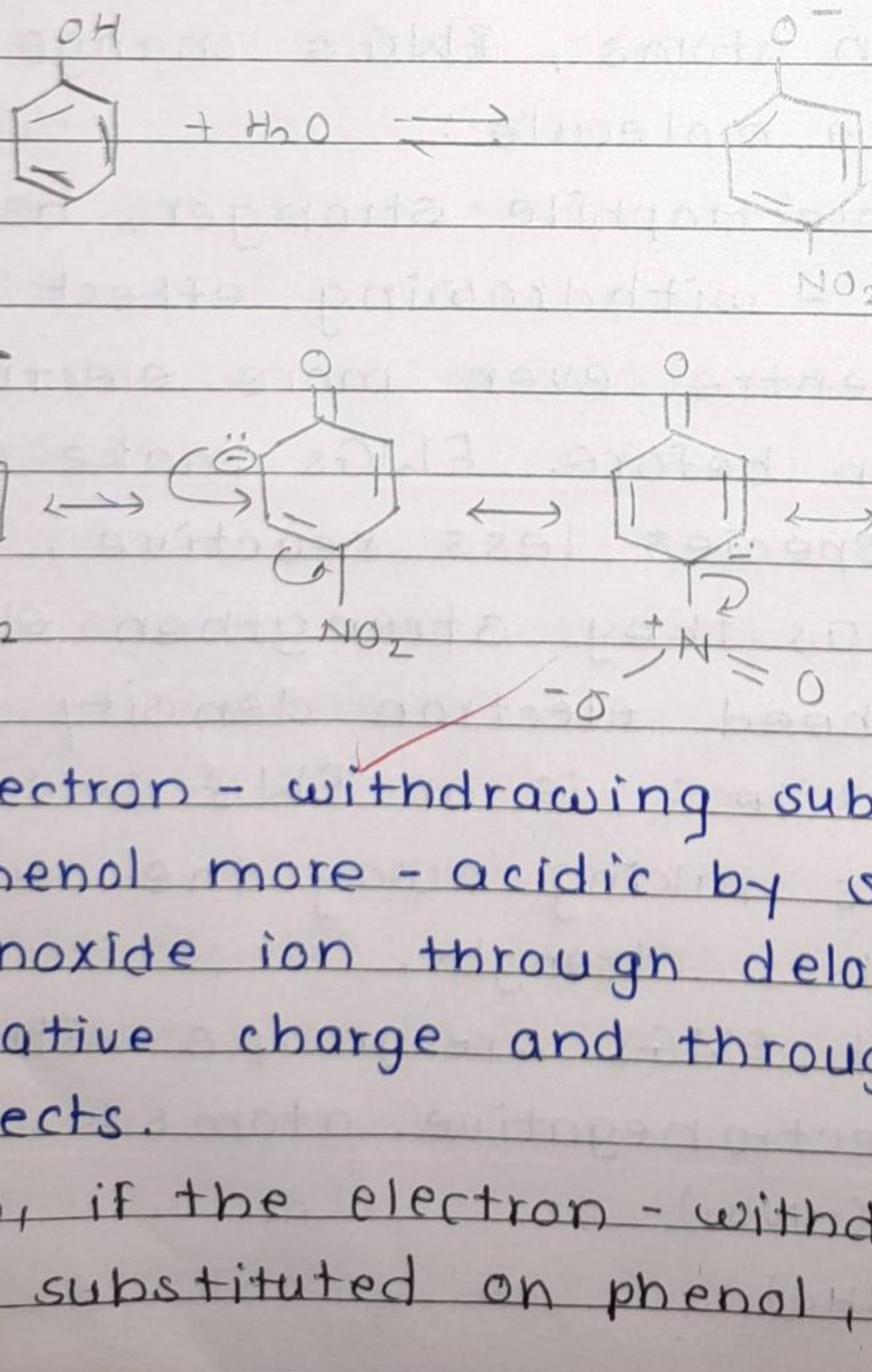
Nitro groups ($-NO_2$)

Aldehyde ($-CHO$)

ketones (- C = OR)
Cyano group (- CN)
Carboxylic acid (- COOH)
Esters (- COOR)
Halogens are also electron withdrawing the effect gets weaker going down the group.

Effect of electron withdrawing group on acidity of phenol compound -

The electron - withdrawing groups are substituted phenol ; they pull the electrons from the negatively charged O, which increases the stability of the phenoxide ion.



Electron - withdrawing substituents make a phenol more - acidic by stabilizing the phenoxide ion through delocalization of the negative charge and through inductive effects.

So, if the electron - withdrawing groups, are substituted on phenol, it increases

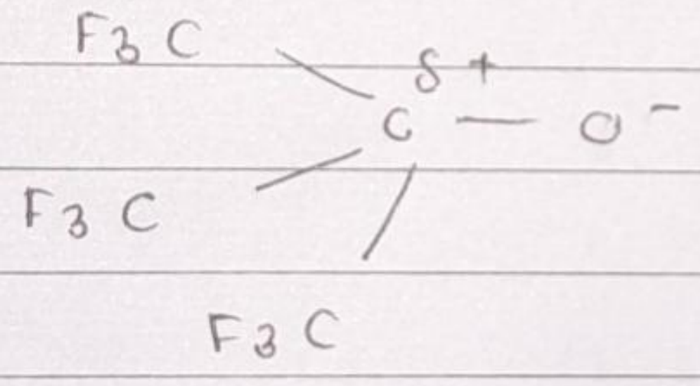
its acidity. Because of this, nitrophenol is more acidic than other rest of the compound so it is should be 4th place in preference.

Que-7 Write the factors affecting acidity of phenol compound ?

Factors that influence acidity :

Inductive effect -

CH_3CH_2OH	FCH_2CH_2OH	F_2CHCH_2OH	F_3CCH_2OH
16.0	14.4	13.3	12.4



A benzene ring is genrally considered electron withdrawing and stabilize the negative charge through inductive effects.

Resonance effect : the benzene ring stabilize the phenoxide ion by resonance delocalisation of the negative charge.

from the above conclusion the correct ans is option-3.

Pune District Education Association's
Seth GovindRaghunath Sable College of Pharmacy, Saswad

Attendance of First Year B. Pharm. Students for PBL-1 2020 – 2021

POC-I

30/07/2024

Roll No.	Name of Students	Email	Attendance
1	Pratik Inamke	Pratikinamke3635@gmail.com	Patil
2	Srushti Jadhav	SrushtiJadhav1909@gmail.com	Jadhav
3	Gaurav Jagtap	Jagtapgavrav812@gmail.com	Jagtap
4	Pradnya Jagtap	pradnyajagtap1901@gmail.com	Jagtap
5	Prakruti Jagtap	prakrutijagtap@gmail.com	Jagtap
6	Shivini Jagtap	Shivinijagtap561@gmail.com	Jagtap
7	Swapnil Jagtap	Swapniljagtap862@gmail.com	Jagtap
8	Riya Jambhale		
9	Aditi Jogdand	aditijagdand143@gmail.com	present.
10	Geetanjali Kad	kadgeetanjali@gmail.com.	Kad

My
(Mr. J. R Jagtap)

Pune District Education Association's
Seth Govind Raghunath Sable College of Pharmacy, Saswad

Feedback of students on PBL conducted on **30/07/2021**

Subject: Pharmaceutical Organic Chemistry-I **Class:** F. Y. B. Pharm. (Sem.-II)

This questionnaire has been designed to understand the opinion of students involved in the PBL activity so that the activity can be improved in the future. The group leader is advised to answer the questions on behalf of all the group members.

Please **tick** the appropriate box:

Trigger	Yes	No	Can't say
Was the trigger provided to you easily understandable?	✓		
Was the trigger interesting?	✓		
Could you relate the trigger to your curriculum?	✓		
Role of facilitator			
Did you find the role of facilitator useful in understanding the problem?	✓		
Did you take the help of the facilitator in identifying the objectives of the problem?	✓		
Resources			
Did you refer to the books available in the library for compiling the data related to your problem?	✓		
Were there sufficient reference books available in the library for researching the problem?	✓		
Did you find the internet facility and online resources adequate?	✓		
Overall activity			
Do you think PBL is enhancing your comprehension and analytical skills?	✓		
Do you think PBL is enhancing your referencing & researching skills?	✓		
Do you think PBL is contributing towards improving your communication and presentation skills?	✓		
Do you think this activity should be continued in future also?	✓		

Suggestions if any ---- -

----------Pl. tear from here before submitting----------

Name of the group leader- ..Jagtap....Pradnya Navnath.

Signature.....

Group No.: 3 (2130)

My
(Mrs. J. R. Jagtap)

Pune District Education Association's

Seth Govind Raghunath Sable College of Pharmacy, Saswad.

PBL No.: 1

FACILITATOR ASSESSMENT FORM

Subject: Pharmaceutical Organic Chemistry-I Date: 30/07/2021

Cass: F. Y. B. Pharm. (Sem.-II)

Please rate in the 5 point scale: 5- Excellent, 4- Very Good, 3- Good, 2- Satisfactory, 1 - Not satisfactory

Roll No. of the student / Criteria	21	22	23	24	25	26	27	28	29	30
Application of knowledge base										
Applies previous knowledge to clarify and define the problem.	5	5	5	5	5	5	5		5	5
Answers questions and shares his/her opinions by applying acquired knowledge.	5	5	5	5	5	5	5		5	5
Critical Thinking										
Demonstrate, evidence, critical understanding and critical analysis facts.	5	4	4	5	4	5	5		5	4
Is applicable making conclusion and decision regarding the diagnostic / therapeutic approaches?	5	5	5	5	5	5	5		5	5
Demonstrates evidence of following a sequential analysis of the problem.	5	5	5	5	5	5	5		5	5
Self Directed Learning(Self study)										
Defines learning objectives and learning goals.	5	5	5	5	5	4	4		5	5
Demonstrates evidence of accomplishment of learning objectives.	5	5	4	5	5	5	5		5	5
If necessary, seeks counseling to orient His/her study and willing to improve	5	5	5	5	5	5	5		5	5
Collaborative work										
Works towards achievement of the groups learning goals with commitment.	5	5	5	5	5	5	5		5	5
Demonstrates effective interpersonal attributes.	5	5	5	5	4	5	5		5	5
Accepts feedback with openness.	5	5	5	5	5	4	5		5	5
Reacts positively to feedback and criticism.	5	5	5	5	5	5	5		5	5
Stands up for his/her points of view.	5	5	5	5	5	5	5		5	5
Shows ability to change his/her point of view of new information given/ obtained.	5	5	5	5	5	5	5		5	5

Signature of Facilitator

Group :- Roll NO. 21+030.

PBL -1 TRIGGER

Class: Second Year B. Pharm. (Sem-III) **Subject: Pharmacology–I**

A taxi driver aged 30 years presented with sudden onset running & itchy nose, bouts of sneezing partial nasal blockage, redness & watering from the eyes, but no fever, bodyache or malaise. He gave history of similar episodes occurring off & on during the spring season. A diagnosis of seasonal allergic rhinitis was made & the doctor decided to prescribe antiallergic medication.

FACILITATOR's NOTES

Learning objectives:

- Which antiallergic medicine would be suitable for this patient?
- Which antiallergic drugs should be avoided?

Compilation of:

1. Synthesis , storage & destruction of Histamine
2. Mechanism of action of Histamine
3. Pathophysiological role of Histamine
4. Classification of Antihistaminics
5. Marketed formulation of histamine & Antihistaminics.

References:

a. Tripathi KD. Essentials of Medical Pharmacology. 7th edition, Jaypee Brothers Medical Publishers (P) Ltd. Page Nos.160-169.

Pune District Education Association's

Seth Govind Raghunath Sable College of Pharmacy, Saswad.

FACILITATOR ASSESSMENT FORM

PBL No.: 1 **Subject: Pharmacology–II**

Please rate in the 5 point scale: 5- Excellent, 4- Very Good, 3-Good, 2- Satisfactory, 1 - Not satisfactory

Criteria \ Roll No. of the student	21	22	23	24	25	26	27	28	29	30
Application of knowledge base										
Applies previous knowledge to clarify and define the problem.	5	4	4	4	3	5	5	4	4	4
Answers questions and shares his/her opinions by applying acquired knowledge.	5	4	4	4	4	3	5	5	4	4
Critical Thinking										
Demonstrate, evidence, critical understanding and critical analysis facts.	5	5	5	4	4	4	5	5	4	4
Is applicable making conclusion and decision regarding the diagnostic / therapeutic approaches?	4	4	4	4	4	4	4	3	4	4
Demonstrates evidence of following a sequential analysis of the problem.	4	4	4	4	4	4	4	4	4	4
Self Directed Learning(Self study)										
Defines learning objectives and learning goals.	4	4	4	4	4	4	4	4	4	4
Demonstrates evidence of accomplishment of learning objectives.	4	4	4	4	4	4	4	4	4	4
If necessary, seeks counseling to orient His/her study and willing to improve	3	3	3	3	4	3	3	4	4	3
Collaborative work										
Works towards achievement of the groups learning goals with commitment.	3	3	3	4	4	4	3	3	4	3
Demonstrates effective interpersonal attributes.	4	4	4	4	4	4	3	3	3	3
Accepts feedback with openness.	4	4	4	4	4	4	4	3	3	3
Reacts positively to feedback and criticism.	3	3	3	3	3	3	3	3	3	3
Stands up for his/her points of view.	4	4	4	4	4	4	4	4	4	4
Shows ability to change his/her point of view of new information given/ obtained.	4	4	4	4	4	4	4	4	4	4

P Bhosale

Signature of Facilitator

(Mr. N. R. Bhosale)

Pune District Education Association's
Seth Govind Raghunath Sable College of Pharmacy, Saswad

Feedback of students on PBL conducted on

Subject: Natural drug technology **Class:** ~~Final~~ Second Year B.Pharm.

This questionnaire has been designed to understand the opinion of students involved in the PBL activity so that the activity can be improved in the future. The group leader is advised to answer the questions on behalf of all the group members.

Please **tick** the appropriate box:

Trigger	Yes	No	Can't say
Was the trigger provided to you easily understandable?	✓		
Was the trigger interesting?	✓		
Could you relate the trigger to your curriculum?	✓		
Role of facilitator			
Did you find the role of facilitator useful in understanding the problem?	✓		
Did you take the help of the facilitator in identifying the objectives of the problem?	✓		
Resources			
Did you refer to the books available in the library for compiling the data related to your problem?	✓		
Were there sufficient reference books available in the library for researching the problem?	✓		
Did you find the internet facility and online resources adequate?	✓		
Overall activity			
Do you think PBL is enhancing your comprehension and analytical skills?	✓		
Do you think PBL is enhancing your referencing & researching skills?	✓		
Do you think PBL is contributing towards improving your communication and presentation skills?	✓		
Do you think this activity should be continued in future also?	✓		

Suggestions if any,----NO.----

----------Pl. tear from here before submitting----------

Name of the group leader..Kharat Akash B.:..Signature.....Bharat.....

Group No.: 8.

Page No.:

Pune District Education Association's

SETH GOVIND RAGHUNATH SABLE COLLEGE OF PHARMACY, SASWAD.

PBL - Trigger

Class :- S.Y. B.Pharm (sem-III) Date :-

sub :- Pharmacology - I

Group participants.

Roll NO.	Names.
21.	Jadhav vaishanvi shivaji
22.	Jagtap sahil sunil
23.	Javalkar Aditya Hanumant
24.	Kale sakshi Ravindra
25.	Kande Tanuja Kondiba
26.	Kawade Anagha Avinash
27.	Khaire Mayuri sunil
28.	Khaire Yogita shailesh
29.	Khaladkar Ruta Vinayak
30.	Kharat Akash Bhagwanrao

1. synthesis. storage & destruction of Histamine.

Ans:. Histamine is β. imidazolylethylamine. It is synthesized locally from the amino acid histidine and degraded rapidly by oxidation and methylation. In mast cell, histamine (positively charged) is held by an acidic protein and heparin (negatively charged) within intracellular granules. When the granules are extruded by exocytosis, Na^+ ions in E.C.F. exchange with histamine to release it free. Increase In intracellular cAMP (caused by β adrenergic agonist and methylxanthines) inhibit histamine release Histamine that is absorbed from the intestine.

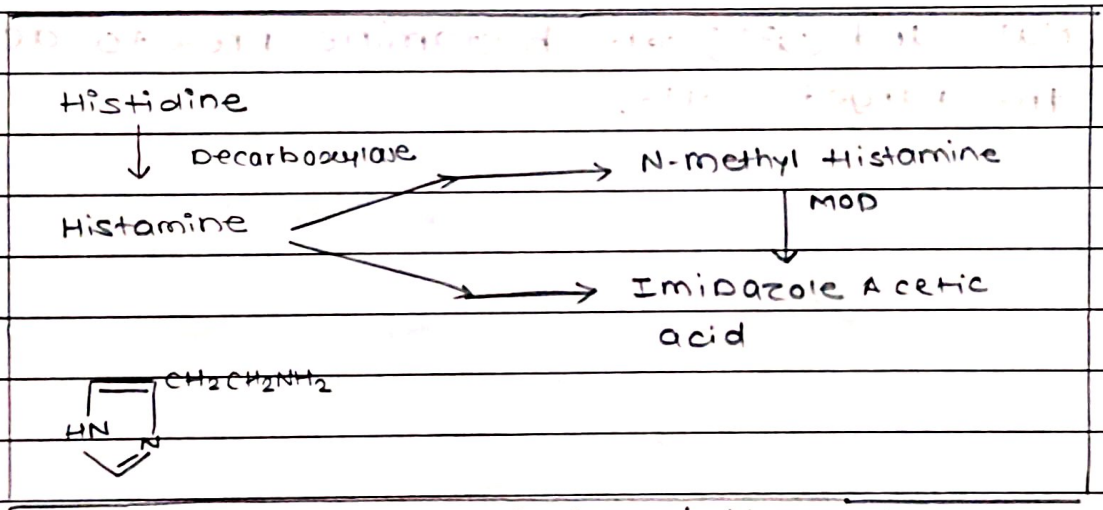


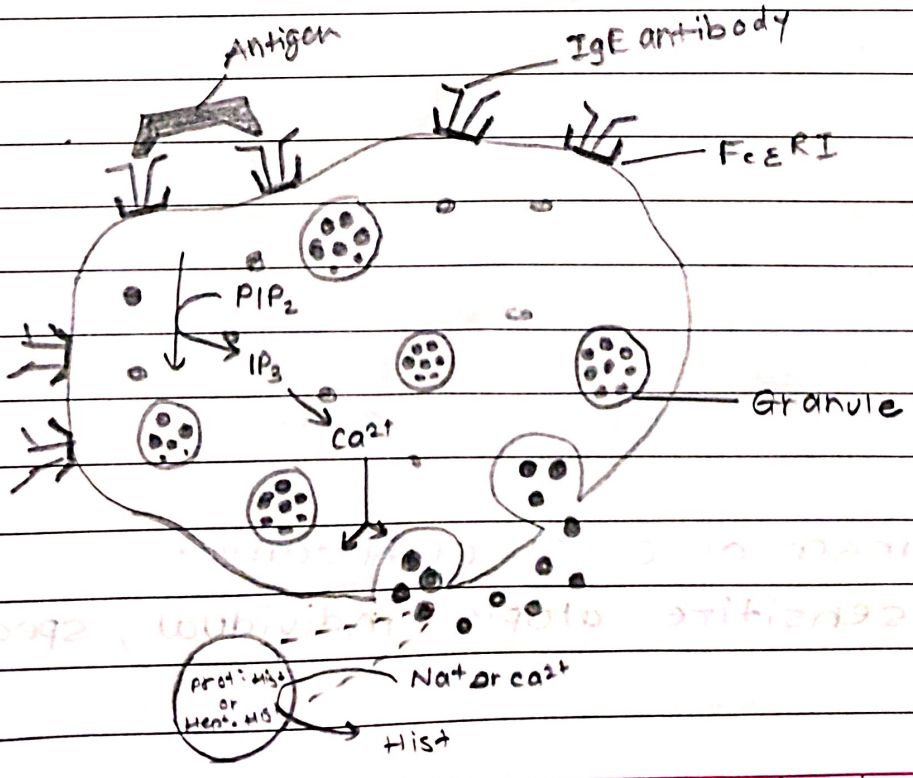
fig. synthesis and degradation of histamine

MAO - monoamine oxidase

2. mechanism of action of Histamine.

Ans:. In sensitive atopic individual, specific reaginic

(IgE) antibody is produced and get bound to fc epsilon receptar I (fcεRI) on the surface of mast cells. on challenge the antigen bridges IgE molecules resulting in transmembrane activation of tyrosine-protein kinase (T-PR-K) which phosphorylates and activate phospholipase Cγ. Phosphatidyl inositol bisphosphate (PIP_2) is hydrolysed and inositol triphosphate (IP_3) is generated which trigger intracellular release of Ca^{2+}. the Ca^{+2} ions induce fusion of granules membrane with plasma membrane of the mast cell resulting in exocytotic release of granule contents. In the granule, positively charged Histamine ($Hist^+$) is held complexed with negatively charged protein ($Prot^-$) and heparin (Hep^-) molecules cationic exchange with extracellular Na^+ (and Ca^{2+}) sets histamine free to acts on the target cells.



Q 3. Pathophysiology role of Histamine :.

1. Gastric secretion :- Histamine has dominant physiological role in mediating secretion of HCl in stomach. Nonmast cell histamine occures in gastric mucosa, possibly in cell called 'histaminocytes' situated closed to the parietal cell, this histamine has high turnover rate. It is released locally under the influence of all stimuli that evoke gastric secretion and activates the proton pump (H^+K^+ ATPase through H_2 receptors)

2. Allergic phenomena :-

mediation of hypersensitivity reaction was the frist role ascribed to histamine. It is an important but only one of mediators of such phenomena. Released from mast cell following AG:AB reaction on their surface (involving IgE type of reginic antibodies) in immediate type of hypersensitivity reaction, histamine is causative in urticaria, angioedma, bronchoconstriction and anaphylatic shock.

② As transmitter :-

Histamine is believed to be the afferent transmitter which initiates the sensation of itch and pain at sensory nerer endings.

Nonmast cell histamine occures in brain, especially hypothalamus and midbrain. It is involved in maintaining wakefulness; H_1 antihistaminics owe their sedative action to blockade of this function. In the brain H_1

promoting action of certain H_1 antagonist,

④ Inflammation :-

Histamine is a mediator of vasodilation and other changes that occure during inflametion. It promotes adhesion of leukocytes to vascular endothelium by expressing adhesion molecules P-selection on endothelial cell surface, sequestrating leukocytes at the inflametion site It may also regulate microcirculation according to local needs

⑤ Tissue growth and repair :-

Because growing and regenerating tissue contain high concentration of histamine, it has been suggested to play an essential role in the process of growth & repair

⑥ Headache :-

Histamine has been implicated in certain vascular headaches, but there is no conclusive evidence.

Q.4. Classification of Antihistaminics.

Ans :-

Clinical classification, dose and preparation of H_1 antihistaminics.

① Highly sedative :-

- Diphenhydramine - Dose 25-50mg. route- oral

- Dimenhydrnate	25-50 mg	oral
- promethazine	25-50 mg	oral
- Hydroxyzine	25-50 mg	oral

② moderately sedative :-

- Pheniramine	25-50 mg	oral
- cyproheptadine	4 mg	oral
- meclozine	25-50 mg	oral
- cinnarizine	25-50 mg	oral

③ mild sedative

- chlorpheniramine	2-4 mg	oral
- Dexchlorphniramine	2 mg	oral
- triprolidine	2.5-5 mg	oral
- clemastine	1-2 mg	oral

④ second generation antihistaminics.

- fexofenadine	120-180 mg	oral
- laratadine	10 mg	oral
- Desloratadine	5 mg	oral
- cetirizine	10 mg	oral
- levocetrizine	5-10 mg	oral
- Azelastine	4 mg	oral
- mitolastine	10 mg	oral
- Ebastine	10 mg	oral
- Rupatadine	10 mg	oral.

Q.5. Marketed formulation of histamine & antihistamine.

Ans:- ① Fexofenadine :-

It is active metabolilite of terfendin

Fexofenadine does not cross blood-brain barrier. does not produce sedation or impair psychomotor performance
Dose:- For allergic rhinitis 120 mg, OD. for urtearia and ther skin allergies 180 mg OD

② Loratadine :-

Another long-active selective peripheral H_1 antagonist lacks CNS depressant effectes and is fast acting

③ cetrizine :-

It is a metabolite or hydroxyzine with marked affinity for peripheral H_1 receptar.