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PRESENCE OF ORGANIC IMPURITIES INTO ACTIVE PHARMACEUTICAL INGREDIENTS: A REVIEW

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ABSTRACT: The presence of excess amount of pharmaceutical impurities in active pharmaceutical ingredients and control of these are a major issue for all pharmaceutical companies. It is very essential to know the presence of impurities in the drug substances and control them up to certain level to avoid adverse effects. Impurities in organic drug molecules can be developed during organic synthesis, formulation or upon aging of active pharmaceutical ingredients, which may affect the quality, safety and efficacy of drugs. Impurity profile is defined as the description of identified and unidentified impurities present in new drugs as per ICH guidelines. The identification of the impurities of different drugs is done by variety of available Chromatographic and Spectroscopic techniques. The different analytical methods are utilized for characterization and identification of impurities such as Capillary Electrophoresis (CE), Gas Chromatography (GC), Supercritical Fluid Chromatography (SFC), Thin Layer Chromatography (TLC), High Performance Thin Layer Chromatography (HPTLC), High Performance Liquid Chromatography (HPLC), UV-Visible, IR, Mass, NMR and Raman spectroscopy. In this review article, study has been done on various well known marketed drugs for their organic impurities, those were reported by various researchers and a list of few drugs is prepared, those were obtained from British Pharmacopeia 2007.

INTRODUCTION: The quality, safety and efficacy of drug products are directly dependent on their toxicological properties and the presence of impurities. Various regulatory authorities like ICH, USFDA, Canadian Drug and Health Agency are emphasizing on the significance of purity detection and the identification of impurities in Active Pharmaceutical Ingredients.

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Biological safety can be achieved by evaluating and obtaining data on presence of impurities in drug substances. That's why impurity profiling is required to get appropriate result from drug substances [1]. The term 'impurity' can be defined as something that is impure or makes something else impure in nature. In the field of pharmaceutical sciences, mostly impurities in drug substances mean presence of organic materials, inorganic residues and residual solvents, besides the drug substance. Impurity profile is the description of identified and unidentified impurities present in new drug substances as per ICH guidelines. It includes identification, structure elucidation and quantitative determination of impurities and

degradation products in bulk drug materials and pharmaceutical formulations. It helps in identifying and quantifying the impurities present in drug substances (APIs) or pharmaceutical formulations [1-4].

Impurities have been named differently or classified as follows:

a) Common Impurities: By-products, Degradation products, Interaction products, Intermediates, Penultimate intermediates, Related products, Transformation products.

b) Various Pharmacopeia listed Impurities: Pharmacopoeias of various countries also mention impurities in various sections; Impurities in Official Articles, Ordinary Impurities, Organic Volatile Impurities etc.

c) As per ICH Terminology: According to ICH guidelines, impurities in the drug substances produced by chemical synthesis can broadly be classified into following three categories;

i. Organic Impurities (Process and Drug related)

ii. Inorganic Impurities

iii. Residual Solvents [1]

i) **Organic Impurities:** Organic impurities can arise in APIs or drug product formulations during the manufacturing process or during the storage of drug substances. They may be known, unknown, volatile, or non-volatile compounds with sources including starting materials, intermediates, unintended by-products, and degradation products. They may also arise from racemization, or contamination of one enantiomeric form with another. In all cases they can result in undesired biological activity.

a) Starting materials or intermediates: These are the most common impurities found in every API unless a proper care is taken in every step involved throughout the multi-step synthesis. In Paracetamol bulk, there is a limit test for p-aminophenol, which could be a starting material for one manufacturer or be an intermediate for another.

b) By-products: In synthetic organic chemistry, getting a single end product with 100% yield is very rare; there is always a chance of having by-products. In the case of Paracetamol bulk, diacetylated paracetamol may form as a by-product.

c) Degradation products: Impurities can also be formed by degradation of the end product during manufacturing of bulk drugs, storage or formulation to different dosage forms or aging. The degradation of Penicillins and Cephalosporins is a well-known example of degradation products. The presence of a ß-lactum ring as well as that of an a-amino group in the C6/C7 side chain plays a critical role in their degradation [4, 5].

ii) Inorganic Impurities: Inorganic impurities can arise from raw materials, synthetic additives, excipients and production processes used when manufacturing drug products. Sources of inorganic impurities include manufacturing process reagents such as ligands, catalysts (e.g. platinum group elements), metals derived from other stages of production (e.g. process water and stainless steel reactor vessels), charcoal, and elements derived from other materials used in filtration.

iii) Residual solvents: Residual solvents are the volatile organic chemicals used during the manufacturing process or generated during drug production. A number of organic solvents used in synthesis of pharmaceutical products have toxic or environmentally hazardous properties, and their complete removal can be very difficult [6].

Sources of Impurities: From the preceding discussion, it is clear that impurities can be originated from several sources such as; Crystallization-related impurities, Stereochemistry-related impurities, Residual solvents, Synthetic

intermediates and by-products, Formulation-related impurities, Impurities arising during storage, Method related impurity, Mutual interaction amongst ingredients, Functional group-related typical degradation [1].

Different methods to identify impurities:

1. **Spectroscopic Method:** The UV-Visible, IR, Mass, NMR and Raman spectroscopic methods are routinely being used for characterizing impurities**.**

2. **Separation Method:** Capillary Electrophoresis (CE), Gas Chromatography (GC), Supercritical Fluid Chromatography (SFC), Thin Layer Chromatography (TLC), High Performance Thin Layer Chromatography (HPTLC), High Performance Liquid Chromatography (HPLC) are regularly being used for separation of impurities and degradation products [4].

Identification of impurities by Researchers: Thomas *et al* reported an unknown impurity in the drug Deferasirox. It was detected by HPLC and identified by (LC–ESI–QT/MS/MS). The impurity was confirmed as 2-[3,5-bis(2-hydroxy-phenyl)-[1,2,4]-triazol-1-yl]-benzoic acid [7].

3-[1-(dimethylamino)ethyl]phenyl N-ethyl-N-methyl carbamate N-oxide, Ethyl-methyl-carbamic acid 4-(1-dimethylamino-ethyl)-phenyl ester, ethyl-methyl-carbamic acid 2-(1-dimethylamino-ethyl)-phenyl ester impurities were reported by Thomas *et al* in the drug Rivastigmine tartrate by using HPLC and LC/MS/MS method [8].

Gazdag M *et al* confirmed the presence of 17α-Hydroxy-17-oic acid and 17α,20-Dihydroxy-21-oic acid impurities in Mazipredone by using HPLC-(APCI)-MS and HPLC- diode-array UV method [9].

Makino Y *et al* determined the presence of (1*R*,2*S*)-(1)-ephedrine and (1*S*,2*S*)-(1) pseudoephedrine impurities in bulk Methamphetamine with the help of HPLC using two different columns: a phenyl-β-cyclodextrin- type column and an ODS-type column [10].

Choe S *et al* identified the presence of pharmaceutical impurities such as Acetaminophen, Caffeine, Chlorpheniramine, Phenacetin, Ambroxol etc. in the drug Methamphetamine crystals seized in Korea by using the GC-FID and GC-MS method [11].

The presence of benzaldehyde and benzyl alcohol in the drug Methamphetamine was identified by Kuwayama K *et al* by using the HS-SPME & GC-MS [12].

Trefi S *et al* investigated different impurity profiles in generic Ciprofloxacin formulations collected from different countries by using ^{19}F, ^{1}H and DOSY NMR techniques. The impurities were 7-chloro-1-cyclopropyl-6-fluoro-4-oxo-1,4-dihydroquinoline-3-carboxylic acid (fluoro-quinolonic acid), 1-cyclopropyl-4-oxo-7-(piperazin-1-yl)-1,4-dihydroquinoline-3-carboxylic acid (des-fluoro compound), 7-[(2-aminoethyl)amino]-1-cyclopropyl-6-fluoro-4-oxo-1,4-dihydroquinoline-3-carboxylic acid (ethylenediamine compound) and 7-chloro-1-cyclopropyl-4-oxo-6-(piperazin-1-yl)-1,4-dihydroquinoline-3-carboxylic acid [13].

The presence of impurities in the antiparkinsonian drugs such as Levodopa, Carbidopa, Entacapone were identified by Vemi´c A *et al* by using reversed-phase LC method. The identified impurities were (2S)-2-amino-3-(4-hydroxyphenyl) propanoic acid and (2RS)-2-amino-3-(4-hydroxy-3-methoxyphenyl)propanoic acid for Levodopa, Methyldopa, 3-O-methylcarbidopa for Carbidopa and (2Z)-2-cyano-3-(3,4-dihydroxy-5-nitrophenyl)-N,N-diethyl-2-propenamide, and 3,4-dihydroxy-5-nitrobenzaldehyde for Entacapone [14].

Sun C *et al* reported a novel impurity in bulk drug Eprosartan by a simple and sensitive HPLC/MS^n and NMR method. The identified impurity was 4,4'-(5,5'-(1E,1'E)-3,3-(4,4'-methylenebis (thiophene-4,2-diyl))bis(2-carboxyprop-1-ene-3,1-diyl)bis(2-butyl-1H-imidazole-5,1-diyl))bis (methylene) dibenzoic acid [15].

Zhang D *et al* isolated and identified three impurities 5-((4-fluorobenzyl)amino)-2-oxo-1H-imidazo[4,5-b]pyridine-1,3(2H)-dicarboxylate, diethyl(6-((4-fluorobenzyl)amino)pyridine-2,3-

diyl)dicarbamate and 5-((4-fluorobenzyl)amino)-1H imidazo[4,5-b]pyridin-2(3H)-one in the drug Flupirtine maleate, a centrally acting, non-opioid, nonsteroidal anti-inflammatory analgesic by using MS, ^{1}H,^{13}C, 2D NMR and IR [16].

Kadivar MH *et al* prepared impurity profile on Febuxostat drug substance by LC–MS/MS technique. The impurities were first identified with the help of LC–MS/MS and characterized by IR and NMR. The impurities 2-(3-carbamoyl-4-isobutoxyphenyl)-4-methyl-1,3-thiazole-5-carboxylic acid, 2-[4-(butan-2-yloxy)-3-cyano phenyl]-4-methyl-1,3-thiazole-5-carboxylic acid, 4-methyl-2-[4-(2-methylpropoxy)phenyl]-1,3-thiazole-5-carboxylic acid, 2-(2-methylpropoxy)-5-(4-methyl-1,3-thiazol-2-yl)benzonitrile were found [17].

Volk KJ *et al* mentioned the presence of impurities such as Norbutorphanol, 9-hydroxy-butorphanol, 9-keto-butorphanol, Ring-contracted butorphanol, Δ1, 10*a*-butorphanol in the drug Butorphanol tartrate by using LC-MS & LC-Tandem MS [18].

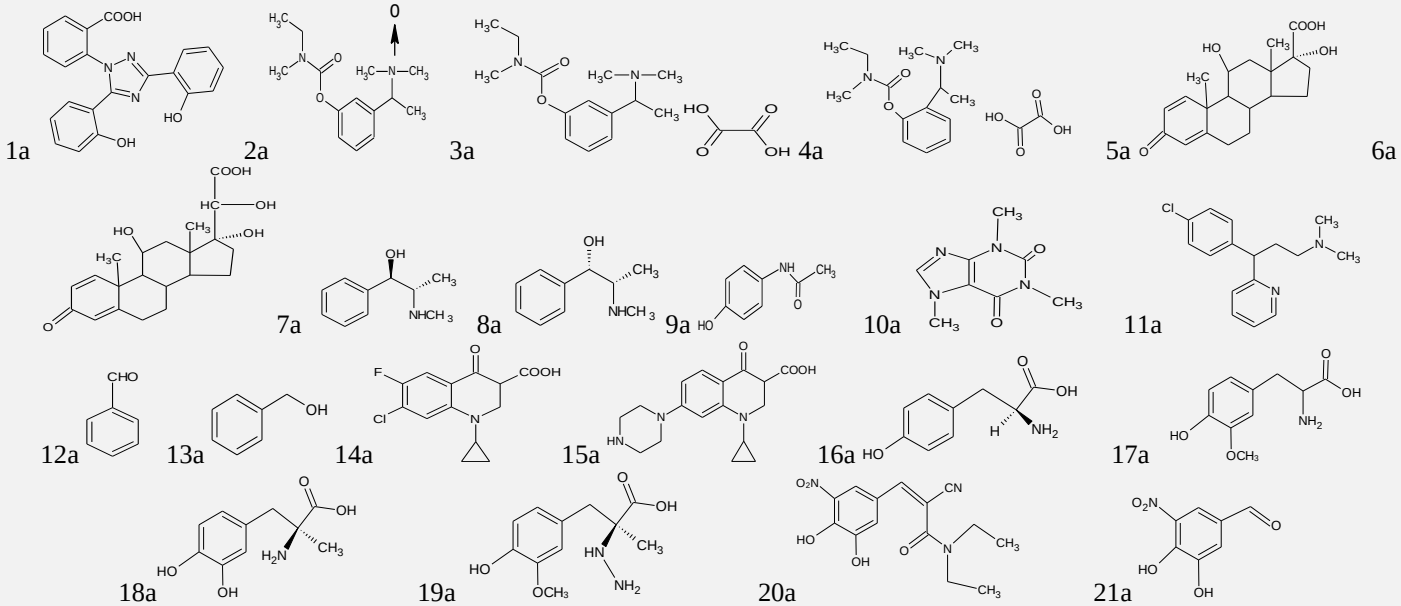
A list of several impurities present in various drugs identified by different methods is shown in **Table 1** and a list of some well-known marketed drugs and their impurities mentioned in British Pharmacopoeia [19] is discussed in **Table 2**.

The structures of the aforementioned impurities are shown in **Figure 1**.

TABLE 1: LIST OF IMPURITIES IDENTIFIED BY DIFFERENT METHODS

Author	Method	Drug	Impurity	Structure
Thomas S *et al* [7]	HPLC & (LC–ESI–QT/MS/MS)	Deferasirox	i)2-[3,5-bis(2-hydroxy-phenyl)-[1,2,4]-triazol-1-yl]-benzoic acid	1a
Thomas S *et al* [8]	HPLC & LC/MS/MS	Rivastigmine tartrate	ii)3-[1-(dimethylamino)ethyl]phenyl N-ethyl-N-methyl carbamate N-oxide iii)Ethyl-methyl-carbamic acid 4-(1-dimethylamino-ethyl)-phenyl ester iv)ethyl-methyl-carbamic acid 2-(1-dimethylamino-ethyl)- phenyl ester	2a 3a 4a
Gazdag M *et al* [9]	HPLC-(APCI)-MS & HPLC-diode-array UV	Mazipredone	v) 17α-Hydroxy-17-oic acid vi) 17α,20-Dihydroxy-21-oic acid	5a 6a
Makino Y *et al* [10]	HPLC	Methamphetamine	vii) (1*R*,2*S*)-(-)-ephedrine viii) (1*S*,2*S*)-(+)-pseudoephedrine	7a 8a
Choe S *et al* [11]	GC-FID & GC-MS	Methamphetamine	ix) Acetaminophen x) Caffeine xi) Chlorpheniramine	9a 10a 11a
Kuwayama K *et al* [12]	HS-SPME/GC–MS	Methamphetamine	xii) Benzaldehyde xiii) Benzyl alcohol	12a 13a
Trefi S *et al* [13]	^{19}F, ^{1}H & DOSY NMR	Ciprofloxacin	xiv) 7-chloro-1-cyclopropyl-6-fluoro-4-oxo-1,4-dihydroquinoline-3-carboxylic acid (fluoroquinolonic acid) xv) 1-cyclopropyl-4-oxo-7-(piperazin-1-yl)-1,4-dihydroquinoline-3-carboxylic acid (desfluoro compound)	14a 15a

Vemi'c A *et al*[14]	RP-HPLC	Levodopa Carbidopa, Entacapone	xvi) ((2S)-2-amino-3-(4-hydroxyphenyl) propanoic acid xvii) (2RS)-2-amino-3-(4-hydroxy-3-methoxyphenyl)propanoic acid xviii) Methyldopa xix)3-O-methylcarbidopa xx) (2Z)-2-cyano-3-(3,4-dihydroxy-5-nitrophenyl)-N,N-diethyl-2-propenamide xxi) 3,4-dihydroxy-5-nitrobenzaldehyde	16a 17a 18a 19a 20a 21a
Sun C *et al*[15]	HPLC/MS^n & NMR	Eprosartan	xxii) 4,4'-(5,5'-(1E,1'E)-3,3-(4,4'-methylenebis(thiophene-4,2-diyl)) bis (2-carboxyprop-1-ene 3,1-diyl)bis(2-butyl-1H-imidazole-5,1 diyl))bis(methylene)dibenzoic acid	22a
Zhang D *et al*[16]	MS, ^{1}H, ^{13}C, 2D NMR & IR	Flupirtine maleate	xxiii) 5-((4-fluorobenzyl)amino)-2-oxo-1H-imidazo[4,5-b]pyridine-1,3(2H)-dicarboxylate xxiv) diethyl(6-((4-fluorobenzyl)amino)pyridine-2,3-diyl)dicarbamate xxv)5-((4-fluorobenzyl)amino)-1H-imidazo[4,5-b]pyridin-2(3H)-one	23a 24a 25a
Kadivar MH *et al*[17]	LC-MS/MS	Febuxostat	xxvi) 2-(3-carbamoyl-4-isobutoxyphenyl)-4-methyl-1,3-thiazole-5-carboxylic acid xxvii) 2-[4-(butan-2-yloxy)-3-cyanophenyl]-4-methyl-1,3-thiazole-5-carboxylic acid xxviii) 4-methyl-2-[4-(2-methylpropoxy)phenyl]-1,3-thiazole-5-carboxylic acid xxix) 2-(2-methylpropoxy)-5-(4-methyl-1,3-thiazol-2-yl)benzonitrile	26a 27a 28a 29a
Volk KJ *et al*[18]	LC-MS & LC-Tandem MS	Butorphanol tartrate	xxx) Norbutorphanol xxxi) 9-hydroxy-butorphanol xxxii)9-keto-butorphanol xxxiii)Ring-contracted butorphanol xxxiv) Δ1, 10*a*-butorphanol	30a 31a 32a 33a 34a



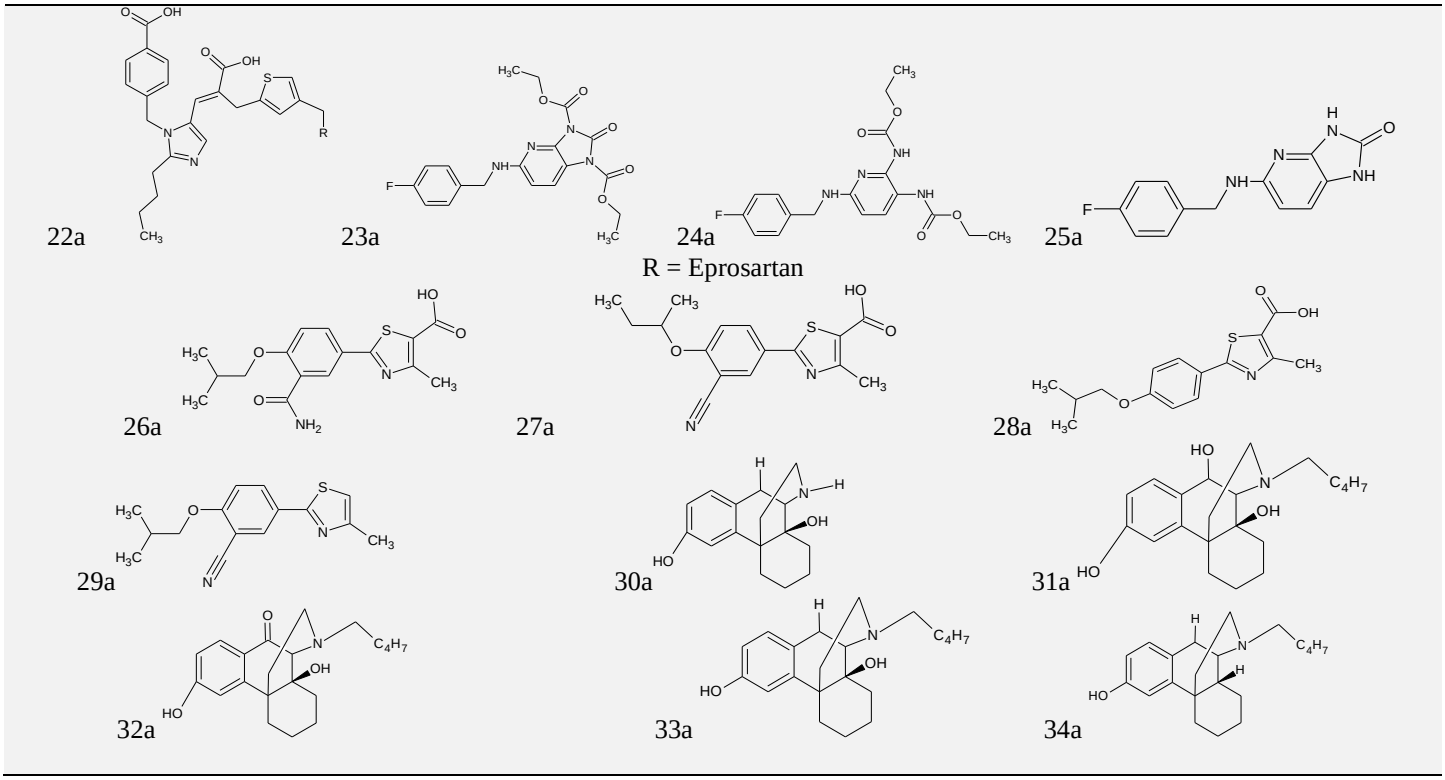
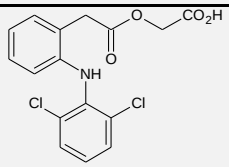
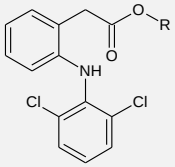
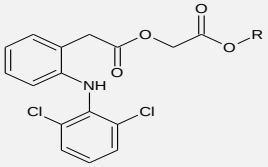
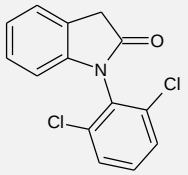


FIGURE 1: STRUCTURE OF IMPURITIES

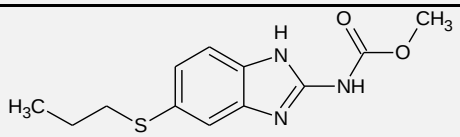
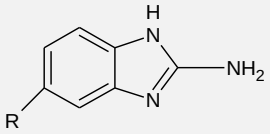
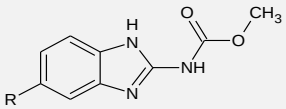
TABLE 2: IMPURITIES OF FEW WELL-KNOWN MARKETED DRUGS AS PER BRITISH PHARMACOPOEIA:

Drug No. 01

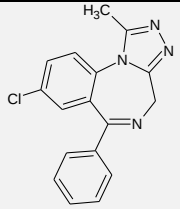
Drug's Name	**Aceclofenac**
Drug's structure	
Activity	Analgesic, Anti-inflammatory
Total impurities	09 (Nine)
Structures of impurities	
Impurity A	R = H: [2-[(2,6-dichlorophenyl)amino]phenyl]acetic acid (diclofenac)
Impurity B	R = CH_3: methyl [2-[(2,6-dichlorophenyl)amino]phenyl]acetate (methyl ester of diclofenac)
Impurity C	R = C_2H_5: ethyl [2-[(2,6-dichlorophenyl)amino]phenyl]acetate (ethyl ester of diclofenac
Impurity D	 R = CH_3: methyl [[[2-[(2,6-dichlorophenyl)amino]phenyl]acetyl]oxy]acetate (methyl ester of aceclofenac)
Impurity E	R = C_2H_5: ethyl [[[2-[(2,6-dichlorophenyl)amino]phenyl]acetyl]oxy]acetate (ethyl ester of

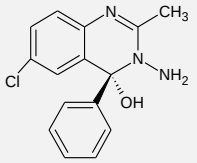
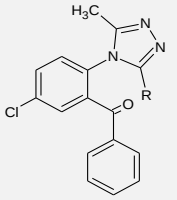
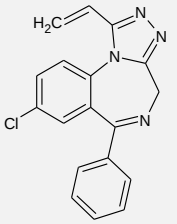
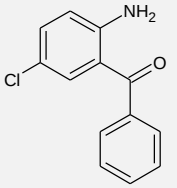
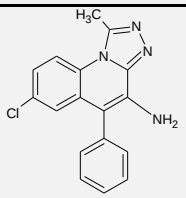
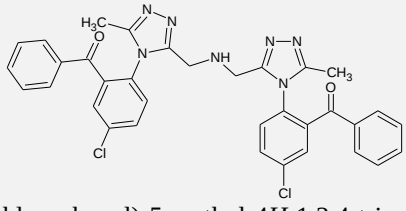
	aceclofenac)
Impurity F	R = CH_2-C_6H_5: benzyl [[[2-[(2,6-dichlorophenyl)amino]phenyl]acetyl]oxy]acetate (benzyl ester of aceclofenac)
Impurity G	R = CH_2-CO_2H: [[[[[2-[(2,6-dichlorophenyl)amino]phenyl]acetyl]oxy]acetyl]oxy]acetic acid (acetic aceclofenac)
Impurity H	R = CH_2-CO-O-CH_2-CO_2H: [[[[[[[2-[(2,6-dichlorophenyl)amino]phenyl]acetyl]oxy]acetyl]oxy]acetyl]oxy]acetic acid (diacetic aceclofenac)
Impurity I	 1-(2,6-dichlorophenyl)-1,3-dihydro-2*H*-indol-2-one

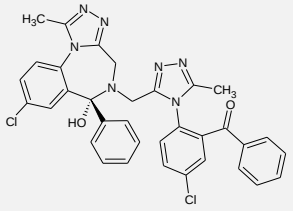
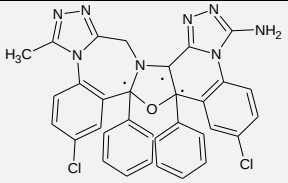
Drug No. 02

Drug's Name	**Albendazole**
Drug's structure	
Activity	Anthelmintic
Total impurities	06 (Six)
Structures of impurities	
Impurity A	R = S-CH_2-CH_2-CH_3: 5-(propylsulphanyl)-1*H*-benzimidazol-2-amine
Impurity D	R = SO_2-CH_2-CH_2-CH_3: 5-(propylsulphonyl)-1*H*-benzimidazol-2-amine
	
Impurity B	R = SO-CH_2-CH_2-CH_3: methyl [5-(propylsulphinyl)-1*H*-benzimidazol-2-yl]carbamate
Impurity C	R = SO_2-CH_2-CH_2-CH_3: methyl [5-(propylsulphonyl)-1*H*-benzimidazol-2-yl]carbamate
Impurity E	R = H: methyl (1*H*-benzimidazol-2-yl)carbamate
Impurity F	R = S-CH_3: methyl [5-(methylsulphanyl)-1*H*-benzimidazol-2-yl]carbamate

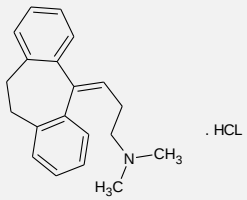
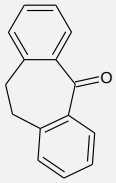
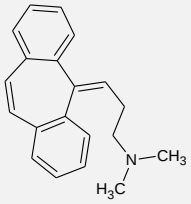
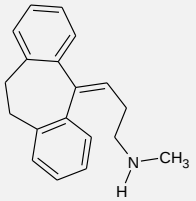
Drug No.03

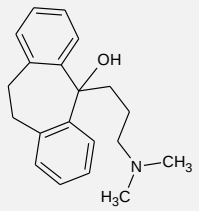
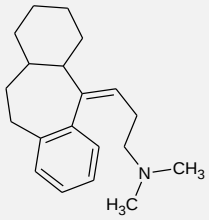
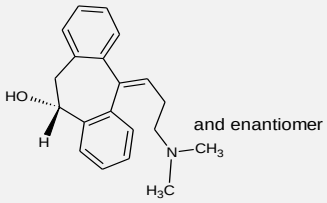
Drug's Name	**Alprazolam**
Drug's structure	
Activity	Anxiolytic

Total impurities	10 (Ten)
Structures of impurities	
Impurity A	and enantiomer (4*RS*)-3-amino-6-chloro-2-methyl-4-phenyl-3,4-dihydroquinazolin-4-ol
	
Impurity B	R = CH_2OH: [5-chloro-2-[3-(hydroxymethyl)-5-methyl-4*H*-1,2,4-triazol-4-yl]phenyl]phenylmethanone
Impurity C	R = H: [5-chloro-2-[3-methyl-4*H*-1,2,4-triazol-4-yl]phenyl]phenylmethanone
Impurity F	R = CH_2Cl: [5-chloro-2-[3-(chloromethyl)-5-methyl-4*H*-1,2,4-triazol-4-yl]phenyl]phenylmethanone
	
Impurity D	8-chloro-1-ethenyl-6-phenyl-4*H*-[1,2,4]triazolo[4,3-*a*][1,4]benzodiazepine
	
Impurity E	(2-amino-5-chlorophenyl)phenylmethanone
	
Impurity G	7-chloro-1-methyl-5-phenyl[1,2,4]triazolo[4,3-*a*]quinolin-4-amine
	
Impurity H	bis[[4-(2-benzoyl-4-chlorophenyl)-5-methyl-4*H*-1,2,4-triazol-3-yl]methyl]amine

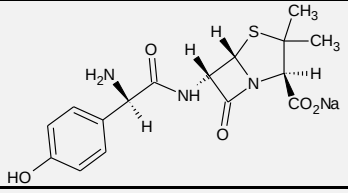
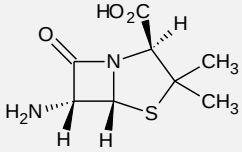
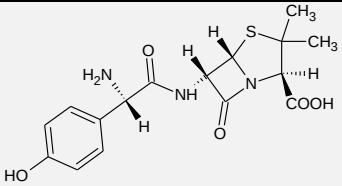
Impurity I	 and enantiomer [5-chloro-2-[3-[[(6*RS*)-8-chloro-6-hydroxy-1-methyl-6-phenyl-4*H*-[1,2,4]triazolo[4, 3-*a*][1,4]benzodiazepin-5(6*H*)-yl]methyl]-5-methyl-4*H*-1,2,4-triazol-4-yl]phenyl]phenylmethanone
Impurity J	 2,17-dichloro-6,13-dimethyl-18b,19a-diphenyl-8b,19a-dihydro-10*H*,18b*H*-[1,2, 4]triazolo[4’’’,3’’’:1’’,2’’]quinolo[3’’,4’’:4’,5’]oxazolo[3’,2’-*d*]-1,2,4-triazolo[4,3-*a*][1,4]benzodiazepine.

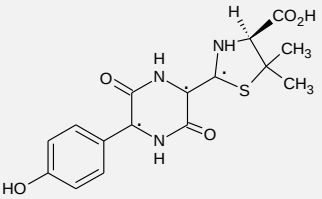
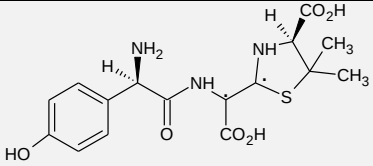
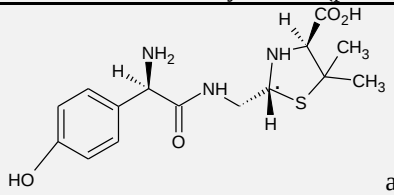
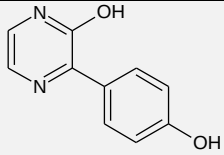
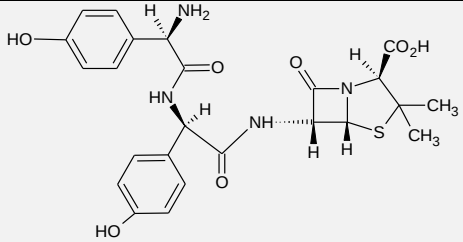
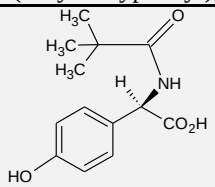
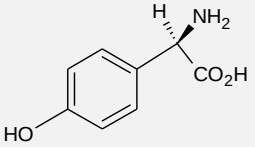
Drug No.04

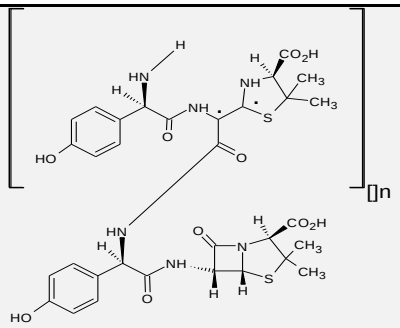
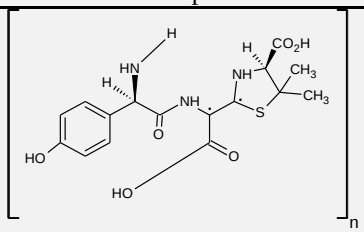
Drug’s Name	**Amitryptyline Hydrochloride**
Drug’s structure	
Activity	Antidepressant
Total impurities	06 (Six)
Structures of impurities	
Impurity A	 10,11-dihydro-5*H*-dibenzo[*a*,*d*][7]annulen-5-one (dibenzosuberone)
Impurity B	 3-(5*H*-dibenzo[*a*,*d*][7]annulen-5-ylidene)-*N*,*N*-dimethylpropan-1-amine (cyclobenzaprine)
Impurity C	 3-(10,11-dihydro-5*H*-dibenzo[*a*,*d*][7]annulen-5-ylidene)-*N*-methylpropan-1-amine

Impurity D	 5-[3-(dimethylamino)propyl]-10,11-dihydro-5*H*-dibenzo[*a*,*d*][7]annulen-5-ol
Impurity E	 3-(1,2,3,4,4a,10,11,11a-octahydro-5*H*-dibenzo[*a*,*d*][7]annulen-5-ylidene)-*N*,*N*-dimethylpropan-1-amine
Impurity F	 (10*RS*)-5-[3-(dimethylamino)propylidene]-10,11-dihydro-5*H*-dibenzo[*a*,*d*] [7]annulen-10 ol

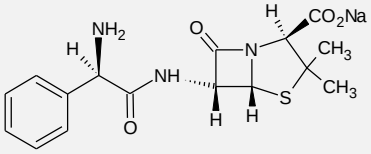
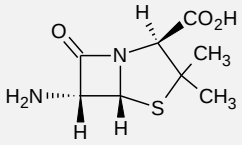
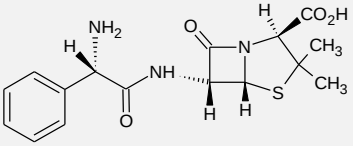
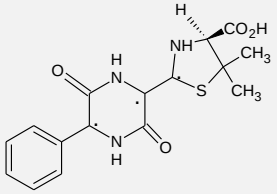
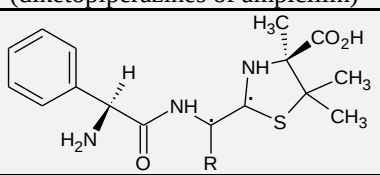
Drug No.05

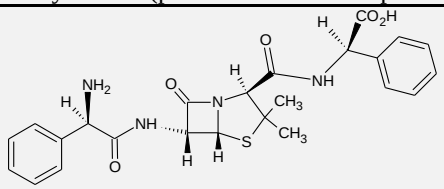
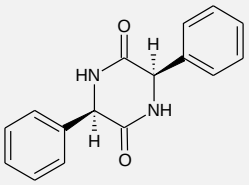
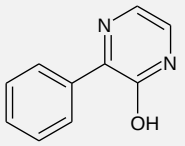
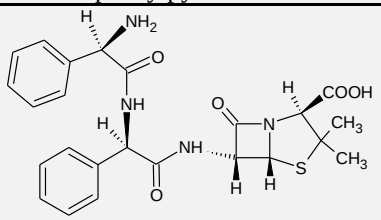
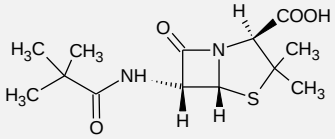
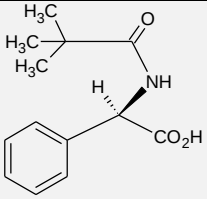
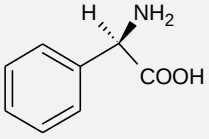
Drug's Name	**Amoxicillin Sodium**
Drug's structure	
Activity	Antibacterial
Total impurities	11 (Eleven)
Structures of impurities	
Impurity A	 (2*S*,5*R*,6*R*)-6-amino-3,3-dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0]heptane-2-carboxylic acid (6-aminopenicillanic acid)
Impurity B	 (2*S*,5*R*,6*R*)-6-[[(2*S*)-2-amino-2-(4-hydroxyphenyl)acetyl]amino]-3,3-dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0]heptane-2-carboxylic acid (L-amoxicillin)

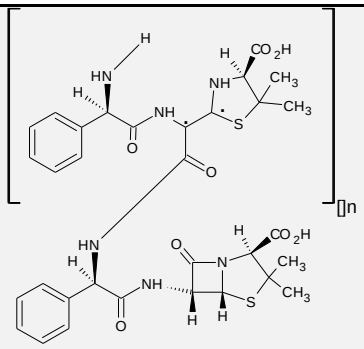
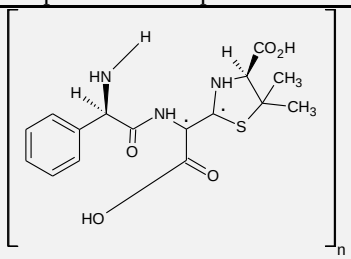
Impurity C	 (4*S*)-2-[5-(4-hydroxyphenyl)-3,6-dioxopiperazin-2-yl]-5,5-dimethylthiazolidine-4-carboxylic acid (amoxicillin diketopiperazines)
Impurity D	 (4*S*)-2-[[[(2*R*)-2-amino-2-(4-hydroxyphenyl)acetyl]amino]carboxymethyl]-5,5-dimethylthiazolidine-4-carboxylic acid (penicilloic acids of amoxicillin)
Impurity E	 and epimer at C* (2*RS*,4*S*)-2-[[[(2*R*)-2-amino-2-(4-hydroxyphenyl)acetyl]amino]methyl]-5,5-dimethylthiazolidine-4-carboxylic acid (penilloic acids of amoxicillin)
Impurity F	 3-(4-hydroxyphenyl)pyrazin-2-ol
Impurity G	 2*S*,5*R*,6*R*)-6-[[(2*R*)-2-[[(2*R*)-2-amino-2-(4-hydroxyphenyl)acetyl]amino]-2-(4-hydroxyphenyl)acetyl]amino]- 3,3-dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0]heptane-2-carboxylic acid (D-(4-hydroxyphenyl)glycylamoxicillin)
Impurity H	 (2*R*)-2-[(2,2-dimethylpropanoyl)amino]-2-(4-hydroxyphenyl)acetic acid
Impurity I	 (2*R*)-2-amino-2-(4-hydroxyphenyl)acetic acid

Impurity J	 co-oligomers of amoxicillin and penicilloic acids of amoxicillin
Impurity K	 oligomers of penicilloic acids of amoxicillin

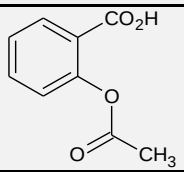
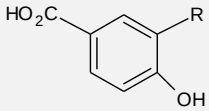
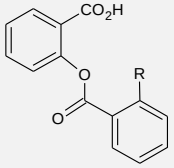
Drug No.06

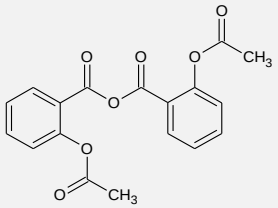
Drug's Name	**Ampicillin Sodium**
Drug's structure	
Activity	Antibacterial
Total impurities	14 (Fourteen)
Structures of impurities **Impurity A**	 (2*S*,5*R*,6*R*)-6-amino-3,3-dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0]heptane-2-carboxylic acid (6-aminopenicillanic acid)
Impurity B	 (2*S*,5*R*,6*R*)-6-[[(2*S*)-2-amino-2-phenylacetyl]amino]-3,3-dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0]heptane-2-carboxylic acid (L-ampicillin)
Impurity C	 (4*S*)-2-(3,6-dioxo-5-phenylpiperazin-2-yl)-5,5-dimethylthiazolidine-4-carboxylic acid (diketopiperazines of ampicillin)
	

Impurity D	R = CO_2H: (4*S*)-2-[[[(2*R*)-2-amino-2-phenylacetyl]amino]carboxymethyl]-5,5-dimethylthiazolidine-4-carboxylic acid (penicilloic acids of ampicillin)
Impurity F	R = H: (2*RS*,4*S*)-2-[[[(2*R*)-2-amino-2-phenylacetyl]amino]methyl]-5,5-dimethylthiazolidine-4-carboxylic acid (penilloic acids of ampicillin)
Impurity E	 (2*R*)-2-[[[(2*S*,5*R*,6*R*)-6-[[(2*R*)-2-amino-2-phenylacetyl]amino]-3,3-dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0]hept-2-yl]carbonyl]amino]-2-phenylacetic acid (ampicillinyl-D-phenylglycine)
Impurity G	 (3*R*,6*R*)-3,6-diphenylpiperazine-2,5-dione
Impurity H	 3-phenylpyrazin-2-ol
Impurity I	 (2*S*,5*R*,6*R*)-6-[[(2*R*)-2-[[(2*R*)-2-amino-2-phenylacetyl]amino]-2-phenylacetyl]amino]-3,3-dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0]heptane-2-carboxylic acid (D-phenylglycylampicillin)
Impurity J	 (2*S*,5*R*,6*R*)-6-[(2,2-dimethylpropanoyl)amino]-3,3-dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0]heptane-2-carboxylic acid
Impurity K	 (2*R*)-2-[(2,2-dimethylpropanoyl)amino]-2-phenylacetic acid
Impurity L	 (2*R*)-2-amino-2-phenylacetic acid (D-phenylglycine)

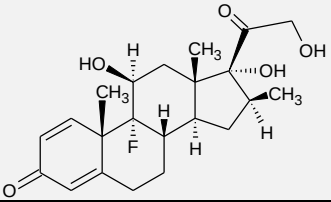
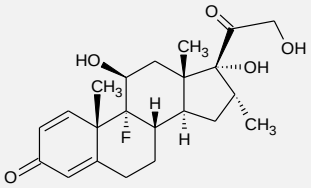
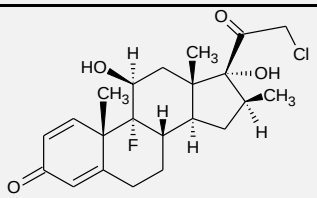
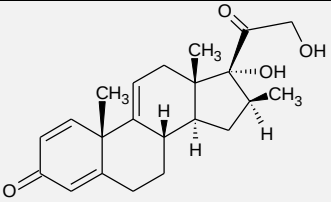
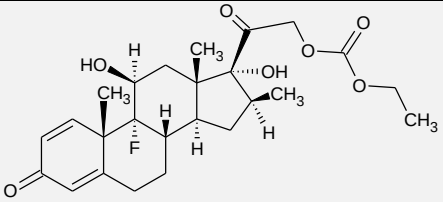
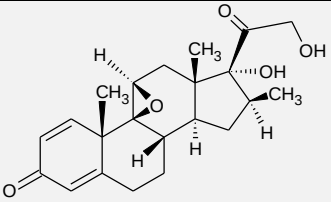
Impurity M	 co-oligomers of ampicillin and of penicilloic acids of ampicillin
Impurity N	 oligomers of penicilloic acids of ampicillin

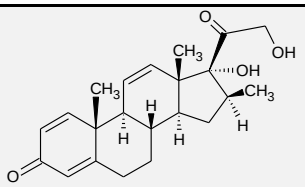
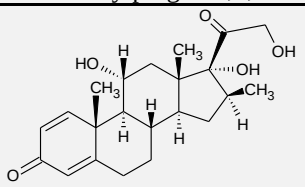
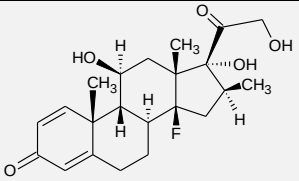
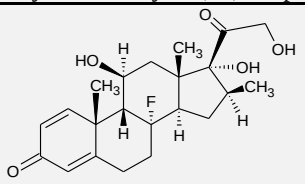
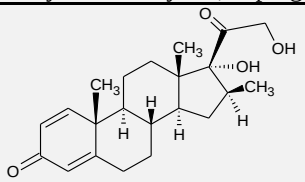
Drug No.07

Drug's Name	**Aspirin**
Drug's structure	
Activity	Analgesic, antipyretic
Total impurities	06 (Six)
Structures of impurities **Impurity A**	 R = H: 4-hydroxybenzoic acid
Impurity B	R = CO_2H: 4-hydroxybenzene-1,3-dicarboxylic acid (4-hydroxyisophthalic acid)
Impurity C	salicylic acid
Impurity D	 R = O-CO-CH_3: 2-[[2-(acetyloxy)benzoyl]oxy]benzoic acid (acetylsalicylsalicylic acid)
Impurity E	R = OH: 2-[(2-hydroxybenzoyl)oxy]benzoic acid (salicylsalicylic acid)

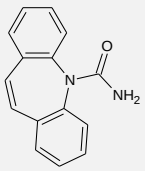
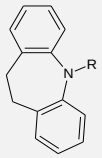
Impurity F	 2-(acetyloxy)benzoic anhydride (acetylsalicylic anhydride)

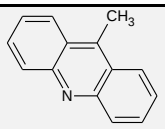
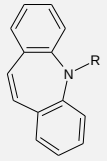
Drug No.08

Drug's Name	**Betamethasone**
Drug's structure	
Activity	Corticosteroid
Total impurities	10 (Ten)
Structures of impurities Impurities A	 Dexamethasone
Impurities B	 21-chloro-9-fluoro-11',17-dihydroxy-16'-methylpregna-1,4-diene-3,20-dione
Impurities C	 17,21-dihydroxy-16'-methylpregna-1,4,9(11)-triene-3,20-dione
Impurities D	 9-fluoro-11',17-dihydroxy-16'-methyl-3,20-dioxopregna-1,4-dien-21-yl ethoxycarboxylate
Impurities E	 9,11'-epoxy-17,21-dihydroxy-16'-methyl-9'-pregna-1,4-diene-3,20-dione

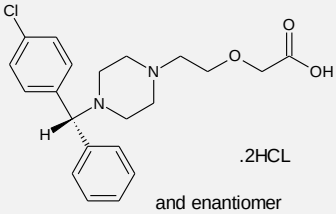
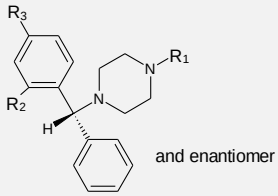
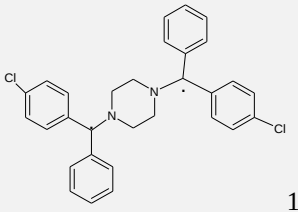
Impurities F	 17,21-dihydroxy-16'-methylpregna-1,4,11-triene-3,20-dione
Impurities G	 11',17,21-trihydroxy-16'-methylpregna-1,4-diene-3,20-dione
Impurities H	 14-fluoro-11',17,21-trihydroxy-16'-methyl-8',9',14'-pregna-1,4-diene-3,20-dione
Impurities I	 8-fluoro-11',17,21-trihydroxy-16'-methyl-8',9'-pregna-1,4-diene-3,20-dione
Impurities J	 17,21-dihydroxy-16□-methylpregna-1,4-diene-3,20-dione

Drug No.09

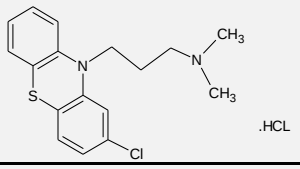
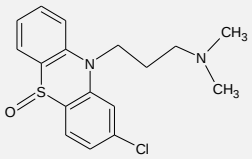
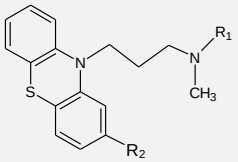
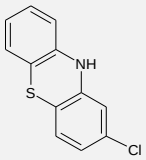
Drug's Name	**Carbamazepine**
Drug's Structure	
Activity	Anticonvulsant
Total Impurities	06 (Six)
Structures of Impurities	
Impurity A	R = $CONH_2$: 10,11-dihydro-5*H*-dibenzo[*b*,*f*]azepine-5-carboxamide (10,11-dihydrocarbamazepine)
Impurity E	R = H: 10,11-dihydro-5*H*-dibenzo[*b*,*f*]azepine(iminodibenzyl)

Impurity B	 9-methylacridine
Impurity C	
Impurity D	R = CO-NH-CO-NH_2: (5*H*-dibenzo[*b,f*]azepin-5-ylcarbonyl)urea(*N*-carbamoylcarbamazepine)
Impurity F	R = H: 5*H*-dibenzo[*b,f*]azepine(iminostilbene) R = CO-Cl: 5*H*-dibenzo[*b,f*]azepine-5-carbonyl chloride (5-chlorocarbonyliminostilbene)

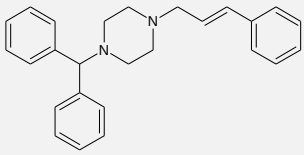
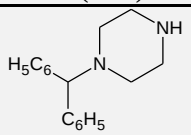
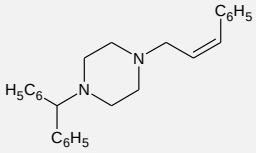
Drug No.10

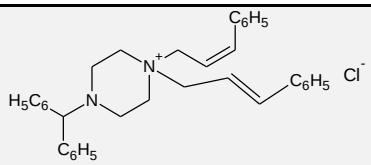
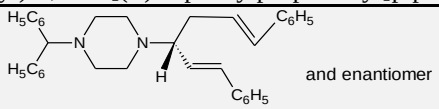
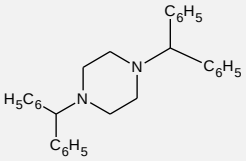
Drug's Name	**Cetirizine Hydrochloride**
Drug's Structure	 .2HCL and enantiomer
Activity	Histamine H_1 receptor antagonist
Total Impurities	07 (Seven)
Structures of Impurities	 and enantiomer
Impurity A	R1 = R2 = H, R3 = Cl: (*RS*)-1-[(4-chlorophenyl)phenylmethyl]piperazine
Impurity B	R1 = CH_2-CO_2H, R2 = H, R3 = Cl: (*RS*)-2-[4-[(4-chlorophenyl)phenylmethyl]piperazin-1-yl]acetic acid
Impurity C	R1 = CH_2-CH_2-O-CH_2-CO_2H, R2 = Cl, R3 = H: (*RS*)-2-[2-[4-[(2-chlorophenyl)phenylmethyl]piperazin-1-yl]ethoxy]acetic acid
Impurity E	R1 = CH_2-[CH_2-O-CH_2]$_2$-CO_2H, R2 = H, R3 = Cl: (*RS*)-2-[2-[2-[4-[(4-chlorophenyl)phenylmethyl]piperazin-1-yl]ethoxy]ethoxy]acetic acid (ethoxycetirizine)
Impurity F	R1 = CH_2-CH_2-O-CH_2-CO_2H, R2 = R3 = H: [2-[4-(diphenylmethyl)piperazin-1-yl]ethoxy]acetic acid
Impurity G	R1 = CH_2-CH_2-OH, R2 = H, R3 = Cl: 2-[4-[(*RS*)-(4-chlorophenyl)phenylmethyl]piperazin-1-yl]ethanol
Impurity D	 1,4-bis[(4-chlorophenyl)phenylmethyl]piperazine

Drug No.11

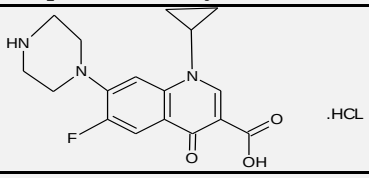
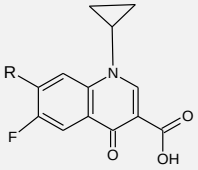
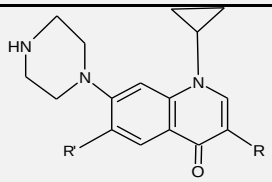
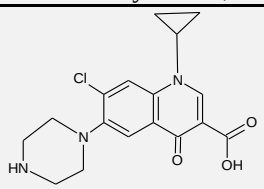
Drug's Name	**Chlorpromazine Hydrochloride**
Drug's Structure	
Activity	Antipsychotic, Anti-emetic
Total Impurities	05 (Five)
Structures of Impurities **Impurity A**	 3-(2-chloro-10*H*-phenothiazin-10-yl)-*N*,*N*-dimethylpropan-1-amine *S*-oxide (chlorpromazine sulphoxide)
Impurity B **Impurity C** **Impurity D**	 R1 = $[CH_2]_3$-N$(CH_3)_2$, R2 = Cl: *N*-[3-(2-chloro-10*H*-phenothiazin-10-yl)propyl]-*N*,*N*',*N*'-trimethylpropane-1,2-diamine R1 = CH_3, R2 = H: promazine R1 = H, R2 = Cl: 3-(2-chloro-10*H*-phenothiazin-10-yl)-*N*-methylpropan-1-amine (desmethylchlorpromazine)
Impurity E	 2-chloro-10*H*-phenothiazine

Drug No.12

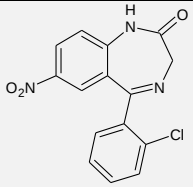
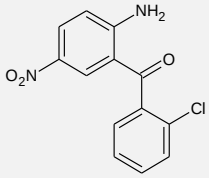
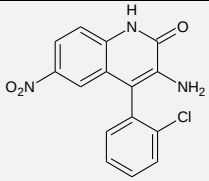
Drug's Name	**Cinnarizine**
Drug's structure	
Activity	Histamine H_1-receptor antagonist.
Total impurities	05 (Five)
Structures of impurities **Impurities A**	 1-(diphenylmethyl)piperazine
Impurities B	 (*Z*)-1-(diphenylmethyl)-4-(3-phenylprop-2-enyl)piperazine

	
Impurities C	(4-(diphenylmethyl)-1,1-bis[(*E*)-3-phenylprop-2-enyl]piperazinium chloride
	 and enantiomer
Impurities D	1-(diphenylmethyl)-4-[(1*RS*,3*E*)-4-phenyl-1-[(*E*)-2-phenylethenyl]but-3-enyl]piperazine
	
Impurities E	1,4-bis(diphenylmethyl)piperazine

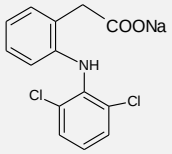
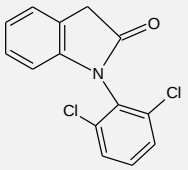
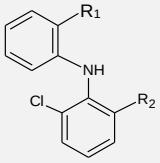
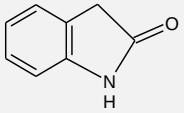
Drug No.13

Drug's Name	**Ciprofloxacin Hydrochloride**
Drug's Structure	 .HCL
Activity	Antibacterial
Total Impurities	06 (Six)
Structures of Impurities	
Impurity A	R = Cl: 7-chloro-1-cyclopropyl-6-fluoro-4-oxo-1,4-dihydroquinoline-3-carboxylic acid (fluoroquinolonic acid)
Impurity C	R = NH-[CH_2]$_2$-NH_2: 7-[(2-aminoethyl)amino]-1-cyclopropyl-6-fluoro-4-oxo-1,4-dihydroquinoline-3-carboxylic acid (ethylenediamine compound)
	
Impurity B	R = CO_2H, R' = H: 1-cyclopropyl-4-oxo-7-(piperazin-1-yl)-1,4-dihydroquinoline-3-carboxylic acid (desfluoro compound),
Impurity E	R = H, R' = F: 1-cyclopropyl-6-fluoro-7-(piperazin-1-yl)quinolin-4(1*H*)-one (decarboxylated compound),
Impurity F	R = CO_2H, R' = OH: 1-cyclopropyl-6-hydroxy-4-oxo-7-(piperazin-1-yl)-1,4-dihydroquinoline-3-carboxylic acid,
	
Impurity D	7-chloro-1-cyclopropyl-4-oxo-6-(piperazin-1-yl)-1,4-dihydroquinoline-3-carboxylic acid.

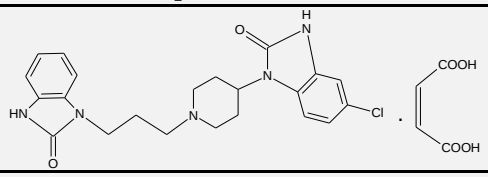
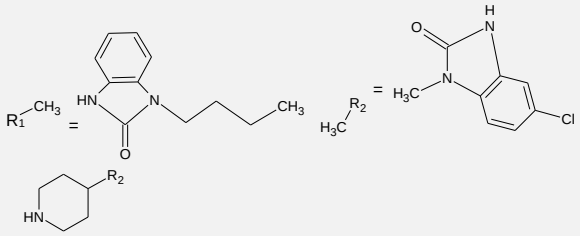
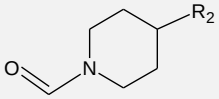
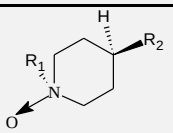
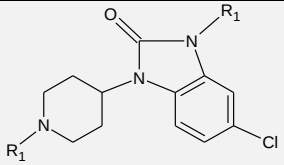
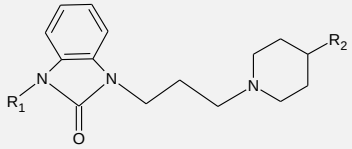
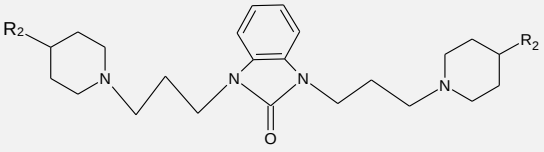
Drug No.14

Drug's Name	**Clonazepam**
Drug's structure	
Activity	Anticonvulsant
Total impurities	02 (Two)
Structures of impurities	
Impurities A	2-amino-5-nitrophenyl)(2-chlorophenyl)methanone
	
Impurity B	3-amino-4-(2-chlorophenyl)-6-nitroquinolin-2(1*H*)-one

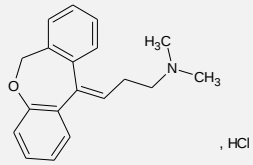
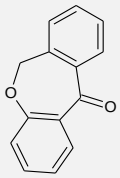
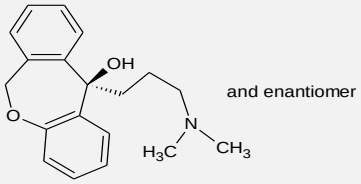
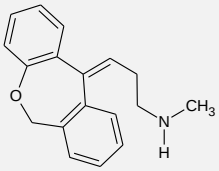
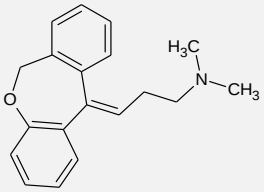
Drug No.15

Drug's Name	**Diclofenac Sodium**
Drug's Structure	
Activity	Analgesic, Anti-inflammatory
Total Impurities	05 (Five)
Structures of Impurities Impurity A	
	1-(2,6-dichlorophenyl)-1,3-dihydro-2*H*-indol-2-one
	
Impurity B	R1 = CHO, R2 = Cl: 2-[(2,6-dichlorophenyl)amino]benzaldehyde,
Impurity C	R1 = CH_2OH, R2 = Cl: [2-[(2,6-dichlorophenyl)amino]phenyl]methanol
Impurity D	R1 = CH_2-CO_2H, R2 = Br: 2-[2-[(2-bromo-6-chlorophenyl)amino]phenyl]acetic acid
	
Impurity E	1,3-dihydro-2*H*-indol-2-one

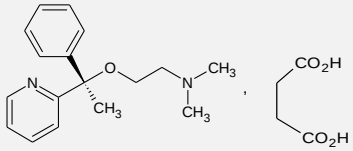
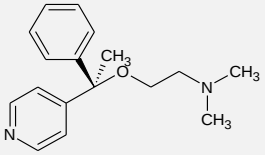
Drug No.16

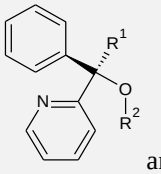
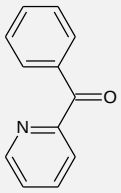
Drug's Name	**Domperidone maleate**
Drug's Structure	
Activity	Antiemetic
Total Impurities	06 (Six)
Structures of Impurities **Impurity A**	 5-chloro-1-(piperidin-4-yl)-1,3-dihydro-2*H*-benzimidazol-2-one
Impurity B	 4-(5-chloro-2-oxo-2,3-dihydro-1*H*-benzimidazol-1-yl)-1-formylpiperidine
Impurity C	 *cis*-4-(5-chloro-2-oxo-2,3-dihydro-1*H*-benzimidazol-1-yl)-1-[3-(2-oxo-2,3-dihydro-1*H*-benzimidazol-1-yl)propyl]piperidine 1-oxide
Impurity D	 5-chloro-3-[3-(2-oxo-2,3-dihydro-1*H*-benzimidazol-1-yl)propyl]-1-[1-[3-(2-oxo-2,3-dihydro-1*H*-benzimidazol-1-yl)propyl]piperidin-4-yl]-1,3-dihydro-2*H*-benzimidazol-2-one
Impurity E	 1-[3-[4-(5-chloro-2-oxo-2,3-dihydro-1*H*-benzimidazol-1-yl)piperidin-1-yl]propyl]-3-[3-(2-oxo-2,3-dihydro-1*H*-benzimidazol-1-yl)propyl]-1,3-dihydro-2*H*-benzimidazol-2-one
Impurity F	 1,3-bis[3-[4-(5-chloro-2-oxo-2,3-dihydro-1*H*-benzimidazol-1-yl)piperidin-1-yl]propyl]-1,3-dihydro-2*H*-benzimidazol-2-one

Drug No.17

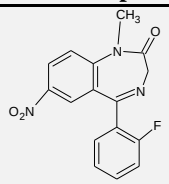
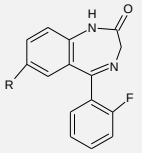
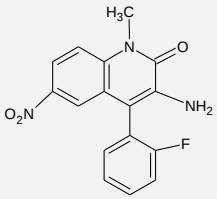
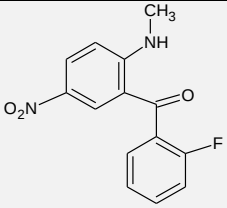
Drug's Name	**Doxepin Hydrochloride**
Drug' structure	
Activity	Antidepressant
Total impurities	04 (Four)
Structures of impurities **Impurities A**	 dibenzo[*b*,*e*]oxepin-11(6*H*)-one
Impurities B	 (11*RS*)-11-[3-(dimethylamino)propyl]-6,11-dihydrodibenzo[*b*,*e*]oxepin-11-ol
Impurities C	 (*E*)-3-(dibenzo[*b*,*e*]oxepin-11(6*H*)-ylidene)-*N*-methylpropan-1-amine
Impurities D	 (*Z*)-3-(dibenzo[*b*,*e*]oxepin-11(6*H*)-ylidene)-*N*,*N*-dimethylpropan-1-amine

Drug No.18

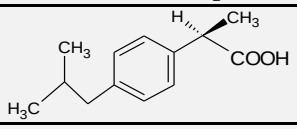
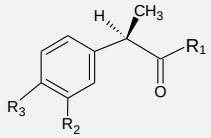
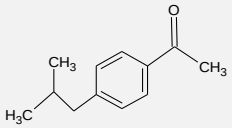
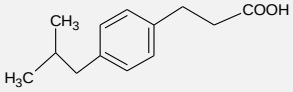
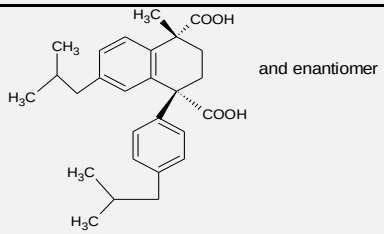
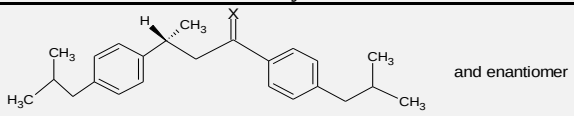
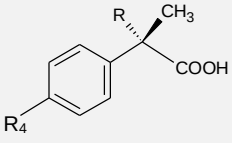
Drug's Name	**Doxylamine Succinate**
Drug's structure	 and enantiomer
Activity	Histamine H_1-receptor antagonist
Total impurities	04 (Four)
Structure of impurities **Impurities A**	 and enantiomer *N*,*N*-dimethyl-2-[1(*RS*)-1-phenyl-1-(pyridin-4-yl)ethoxy]ethanamine

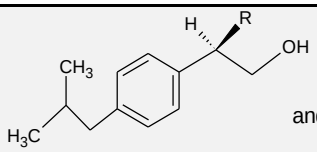
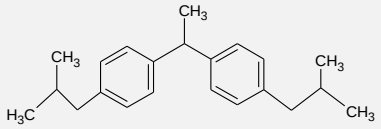
	 and enantiomer
Impurities B	R1 = CH_3, R2 = H: (1*RS*)-1-phenyl-1-(pyridin-2-yl)ethanol
Impurities C	R1 = H, R2 = CH_2-CH_2-N(CH_3)$_2$: *N*,*N*-dimethyl-2-[(*RS*)-1-phenyl(pyridin-2-yl)methoxy]ethanamine
	
Impurities D	Phenyl(pyridin-2-yl)methanone (2-benzoylpyridine)

Drug No.19

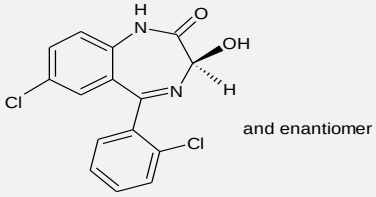
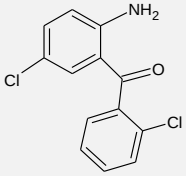
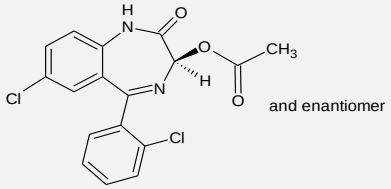
Drug's Name	**Flunitrazepam**
Drug's Structure	
Activity	Hypnotic
Total Impurities	04 (Four)
Structures of Impurities	
Impurity A	R = NH_2: 7-amino-5-(2-fluorophenyl)-1,3-dihydro-2*H*-1,4-benzodiazepin-2-one (7-aminodemethylflunitrazepam)
Impurity B	R = NO_2: 5-(2-fluorophenyl)-7-nitro-1,3-dihydro-2*H*-1,4-benzodiazepin-2-one (demethylflunitrazepam)
Impurity C	 3-amino-4-(2-fluorophenyl)-1-methyl-6-nitroquinolin-2(1*H*)-one
Impurity D	 (2-fluorophenyl)[2-(methylamino)-5-nitrophenyl]methanone

Drug No.20

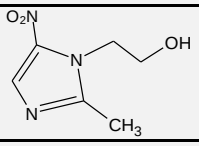
Drug's Name	**Ibuprofen**
Drug's Structure	 and enantiomer
Activity	Analgesic, Anti-inflammatory
Total Impurities	18 (Eighteen)
Structures of Impurities	 and enantiomer
Impurity A	R1 = OH, R2 = CH_2-$CH(CH_3)_2$, R3 = H: (2*RS*)-2-[3-(2-methylpropyl)phenyl]propanoic acid
Impurity B	R1 = OH, R2 = H, R3 = $[CH_2]_3$-CH_3: (2*RS*)-2-(4-butylphenyl)propanoic acid
Impurity C	R1 = NH_2, R2 = H, R3 = CH_2-$CH(CH_3)_2$: (2*RS*)-2-[4-(2-methylpropyl)phenyl]propanamide
Impurity D	R1 = OH, R2 = H, R3 = CH_3: (2*RS*)-2-(4-methylphenyl)propanoic acid
Impurity E	 1-[4-(2-methylpropyl)phenyl]ethanone
Impurity F	 3-[4-(2-methylpropyl)phenyl]propanoic acid
Impurity G	 and enantiomer *cis*-7-(2-methylpropyl)-1-[4-(2-methylpropyl)phenyl]-1,2,3,4-tetrahydronaphthalene-1,4-dicarboxylic acid
Impurity H	 and enantiomer X = O: (3*RS*)-1,3-bis[4-(2-methylpropyl)phenyl]butan-1-one
Impurity I	X = H_2: (3*RS*)-1,3-bis[4-(2-methylpropyl)phenyl]butane
	 and enantiomer
Impurity J	R = H, R4 = CO-$CH(CH_3)_2$: (2*RS*)-2-[4-(2-methylpropanoyl)phenyl]propanoic acid
Impurity K	R = H, R4 = CHO: (2*RS*)-2-(4-formylphenyl)propanoic acid
Impurity L	R = H, R4 = CHOH-$CH(CH_3)_2$: 2-[4-(1-hydroxy-2-methylpropyl)phenyl]propanoic acid
Impurity M	R = OH, R4 = CH_2-$CH(CH_3)_2$: (2*RS*)-2-hydroxy-2-[4-(2-methylpropyl)phenyl]propanoic acid
Impurity N	R = H, R4 = C_2H_5: (2*RS*)-2-(4-ethylphenyl)propanoic acid
Impurity O	R = H, R4 = $CH(CH_3)$-C_2H_5: 2-[4-(1-methylpropyl)phenyl]propanoic acid

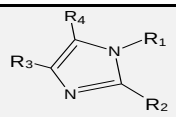
Impurity P **Impurity Q**	 and enantiomer R = CH_3: (2*RS*)-2-[4-(2-methylpropyl)phenyl]propan-1-ol R = H: 2-[4-(2-methylpropyl)phenyl]ethanol
Impurity R	 1,1-bis[4-(2-methylpropyl)phenyl]ethane

Drug No.21

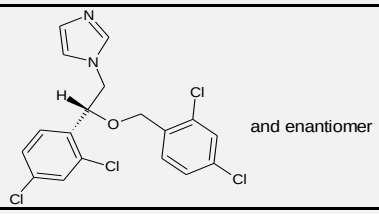
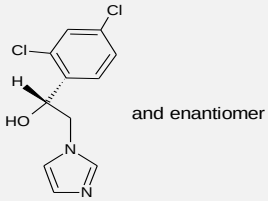
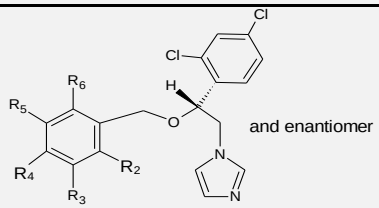
Drug's Name	**Lorazepam**
Drug' structure	 and enantiomer
Activity	Anxiolytic
Total impurities	02 (Two)
Structures of impurities	
Impurities A	(2-amino-5-chlorophenyl)(2-chlorophenyl)methanone,
	 and enantiomer
Impurities B	**(3*RS*)-7-chloro-5-(2-chlorophenyl)-2-oxo-2,3-dihydro-1*H*-1,4-benzodiazepin-3-yl acetate**

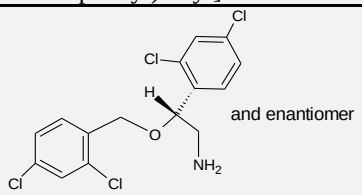
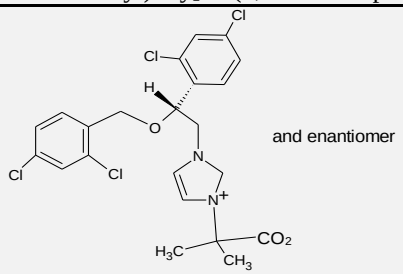
Drug No.22

Drug's Name	**Metronidazole**
Drug's Structure	
Activity	Antibacterial
Total Impurities	07 (Seven)

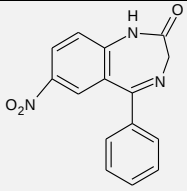
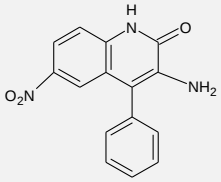
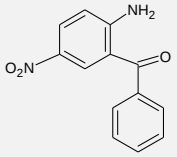
Structures of Impurities	
Impurity A	R1 = R4 = H, R2 = CH_3, R3 = NO_2: 2-methyl-4-nitroimidazole
Impurity B	R1 = R2 = R4 = H, R3 = NO_2: 4-nitroimidazole
Impurity C	R1 = CH_2-CH_2-OH, R2 = R4 = H, R3 = NO_2: 2-(4-nitro-1*H*-imidazol-1-yl)ethanol
Impurity D	R1 = CH_2-CH_2-OH, R2 = R3 = H, R4 = NO_2: 2-(5-nitro-1*H*-imidazol-1-yl)ethanol
Impurity E	R1 = CH_2-CH_2-OH, R2 = CH_3, R3 = NO_2, R4 = H: 2-(2-methyl-4-nitro-1*H*-imidazol-1-yl)ethanol
Impurity F	R1 = CH_2-CH_2-O-CH_2-CH_2-OH, R2 = CH_3, R3 = H, R4 = NO_2: 2-[2-(2-methyl-5-nitro-1*H*-imidazol-1-yl)ethoxy]ethanol
Impurity G	R1 = CH_2-CO_2H, R2 = CH_3, R3 = H, R4 = NO_2: 2-(2-methyl-5-nitro-1*H*-imidazol-1-yl)acetic acid

Drug No.23

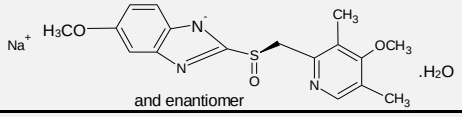
Drug's Name	**Miconazole**
Drug's Structure	 and enantiomer
Activity	Antifungal
Total Impurities	09 (Nine)
Structures of Impurities	 and enantiomer
Impurity A	(1*RS*)-1-(2,4-dichlorophenyl)-2-(1*H*-imidazol-1-yl)ethanol
	 and enantiomer
Impurity B	R2 = R3 = R5 = R6 = H, R4 = Cl: 1-[(2*RS*)-2-[(4-chlorobenzyl)oxy]-2-(2,4-dichlorophenyl)ethyl]-1*H*-imidazole
Impurity D	R2 = R6 = Cl, R3 = R4 = R5 = H: 1-[(2*RS*)-2-[(2,6-dichlorobenzyl)oxy]-2-(2,4-dichlorophenyl)ethyl]-1*H*-imidazole
Impurity F	R2 = R5 = R6 = H, R3 = R4 = Cl: 1-[(2*RS*)-2-[(3,4-dichlorobenzyl)oxy]-2-(2,4-dichlorophenyl)ethyl]-1*H*-imidazole
Impurity G	R2 = R5 = Cl, R3 = R4 = R6 = H: 1-[(2*RS*)-2-[(2,5-dichlorobenzyl)oxy]-2-(2,4-dichlorophenyl)ethyl]-1*H*-imidazole

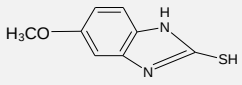
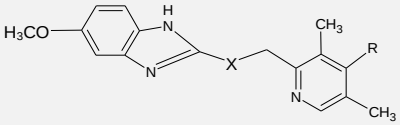
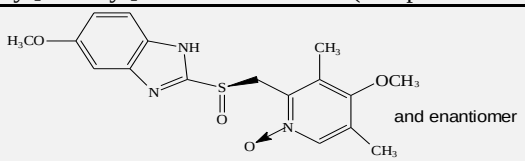
Impurity H	R2 = R3 = R4 = R5 = R6 = H: 1-[(2*RS*)-2-benzyloxy-2-(2,4-dichlorophenyl)ethyl]-1*H*-imidazole
Impurity I	R2 = Cl, R3 = R4 = R5 = R6 = H: 1-[(2*RS*)-2-[(2-chlorobenzyl)oxy]-2-(2,4-dichlorophenyl)ethyl]-1*H*-imidazole
	 and enantiomer
Impurity C	(2*RS*)-2-[(2,4-dichlorobenzyl)oxy]-2-(2,4-dichlorophenyl)ethanamine
	 and enantiomer
Impurity E	2-[1-[(2*RS*)-2-[(2,4-dichlorobenzyl)oxy]-2-(2,4-dichlorophenyl)ethyl]-1*H*-imidazol-3-io]-2-methylpropanoate

Drug No.24

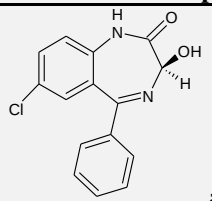
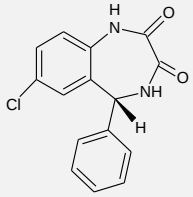
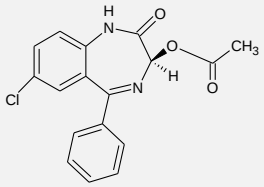
Drug's Name	**Nitrazepam**
Drug's Structure	
Activity	Hypnotic
Total Impurities	02 (Two)
Structures of Impurities **Impurity A**	 3-amino-6-nitro-4-phenylquinolin-2(1*H*)-one
	
Impurity B	**(2-amino-5-nitrophenyl)phenylmethanone**

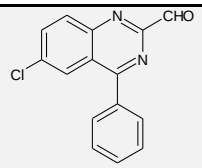
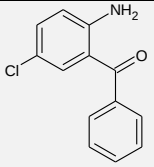
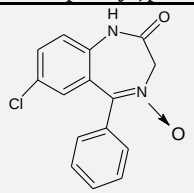
Drug No.25

Drug's Name	**Omeprazole Sodium**
Drug's Structure	 and enantiomer
Activity	Treatment of Peptic ulcer
Total Impurities	05 (Five)

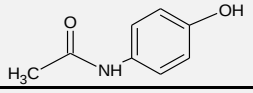
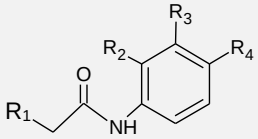
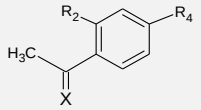
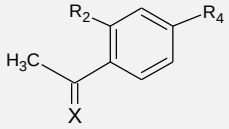
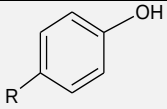
Structures of Impurities	
Impurity A	5-methoxy-1*H*-benzimidazole-2-thiol
Impurity B	 R = H, X = SO: 2-[(*RS*)-[(3,5-dimethylpyridin-2-yl)methyl]sulphinyl]-5-methoxy-1*H*-benzimidazole
Impurity C	R = OCH_3, X = S: 5-methoxy-2-[[(4-methoxy-3,5-dimethylpyridin-2-yl)methyl]thio]-1*H*-benzimidazole (ufiprazole)
Impurity D	R = OCH_3, X = SO_2: 5-methoxy-2-[[(4-methoxy-3,5-dimethylpyridin-2-yl)methyl]sulfonyl]-1*H*-benzimidazole (omeprazole-sulphone)
Impurity E	 and enantiomer 4-methoxy-2-[[(*RS*)-(5-methoxy-1*H*-benzimidazol-2-yl)sulphinyl]methyl]-3,5-dimethylpyridine 1-oxide

Drug No.26

Drug's Name	**Oxazepam**
Drug' structure	 and enantiomer
Activity	Anxiolytic
Total impurities	05 (Five)
Structures of impurities	 and enantiomer
Impurities A	(5*RS*)-7-chloro-5-phenyl-4,5-dihydro-1*H*-1,4-benzodiazepine-2,3-dione
	 and enantiomer
Impurities B	**(3*RS*)-7-chloro-2-oxo-5-phenyl-2,3-dihydro-1*H*-1,4-benzodiazepin-3-yl acetate**

Impurities C	 6-chloro-4-phenylquinazoline-2-carbaldehyde
Impurities D	 (2-amino-5-chlorophenyl)phenylmethanone
Impurities E	 7-chloro-5-phenyl-1,3-dihydro-2*H*-1,4-benzodiazepin-2-one 4-oxide

Drug No.27

Drug's Name	**Paracetamol**
Drug's Structure	
Activity	Analgesic, Antipyretic
Total Impurities	11 (Eleven)
Structures of Impurities	
Impurity A	R1 = R3 = R4 = H, R2 = OH: *N*-(2-hydroxyphenyl)acetamide
Impurity B	R1 = CH_3, R2 = R3 = H, R4 = OH: *N*-(4-hydroxyphenyl)propanamide
Impurity C	R1 = R2 = H, R3 = Cl, R4 = OH: *N*-(3-chloro-4-hydroxyphenyl)acetamide
Impurity D	R1 = R2 = R3 = R4 = H: *N*-phenylacetamide
Impurity H	R1 = R2 = R3 = H, R4 = O-CO-CH_3: 4-(acetylamino)phenyl acetate
Impurity J	R1 = R2 = R3 = H, R4 = Cl: *N*-(4-chlorophenyl)acetamide (chloroacetanilide)
	
Impurity E	X = O, R_2 = H, R_4 = OH: 1-(4-hydroxyphenyl)ethanone
Impurity G	X = N-OH, R_2 = H, R_4 = OH: 1-(4-hydroxyphenyl)ethanone oxime
Impurity I	 X = O, R2 = OH, R4 = H: 1-(2-hydroxyphenyl)ethanone
	
Impurity F	R = NO_2: 4-nitrophenol
Impurity K	R = NH_2: 4-aminophenol

CONCLUSION: Impurity profiling of a pharmaceutical substance under investigation gives maximum possible description of impurities present in it. The establishment of regulatory guidelines for impurity levels in drug substances and products provides the quality criteria for manufacturers. These impurities are developed in the pharmaceutical products during manufacturing process, chemical synthesis, formulation, storage etc. Various analytical tools have been used for the detection, identification and characterization of various impurities in active pharmaceutical ingredients. From the above discussion, it has been observed that there are lots of impurities present in a number of well-known marketed drugs whose successful identification and control of the individual or total content as per pharmacopoeias is needed to render biological safety and efficacy.

The present study throws the attention to the future researchers to set the impurity profiling as a paramount step in the process of quality control and to develop more sophisticated analytical techniques to detect the level of potent impurities present in drugs in a more accurate way. Even in this article, we have tried to give a brief list of impurities of well-known marketed drugs, mentioned into British pharmacopeia. In future, we would like to make more improvised list of impurities with their content limits along with APIs of all well-known marketed drugs, listed in other pharmacopoeias also.

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