CHAPTER 2

LITERATURE SURVEY

This chapter consists of a literature survey review of the research work done for the analysis of genotoxic impurities in drug substances by various analytical tools in line with our proposed research work.

2.1 Literature survey on atazanavir sulphate and impurities

The various analytical techniques for the determination of the atazanavir sulphate and itsimpurities, biological matrices and different combination of drugs have reported by various researchers were included in table 2.1 [42-61]. But there was no analytical methods have been developed for the quantification of BOC epoxide in atazanavir sulphate at low level determination.

Table 2.1: Literature survey on different methods using different liquid chromatography and spectroscopic techniques for atazanavir sulphate and its impurities

S.No	Technique	Analytes	Author/s	Ref
1	RP-HPLC	Active pharmaceutical ingredient	Chitturi et al.	42
2	RP-HPLC	Bulk and dosage form	Bhirud et al.	43
3	RP-HPLC	Bulk and tablet dosage form	Naazneen et al.	44
4	RP-HPLC	Bulk drug	Dey et al.	45
5	RP-HPLC	Bulk and dosage form	Konidala et al.	46
6	RP-HPLC	Pharmaceutical dosage form	Srinivasu et al.	47
7	RP-HPLC	Bulk and formulations	Pawar et al.	48
8	RP-HPLC	Bulk and pharmaceutical dosage form	Panigrahy et al.	49
9	TLC	Bulk drugs	Kuppusamy et al.	50
10	RP-HPLC	Pharmaceutical formulation	Anupama et al.	51
11	Spectrophotometric method	Tablet dosage form	Patel et al.	52
12	Various analytical technique-a review	Atazanavir sulphate	Divya et al.	53

S.No	Technique	Analytes	Author/s	Ref
13	LC-MS	Pripheralblood mononuclear cell lysate	Heine et al.	54
14	LC-MS	Transcriptase inhibitors in dried blood spots	Heine et al.	55
15	HPLC-MS	Plasma	D'Avolio et al.	56
16	HPLC-MS	Human plasma	Dickinson et al.	57
17	LC-MS	Dried blood spot samples	Koal et al.	58
18	LC-MS	Peripheral blood mononuclear cells	Colombo et al.	59
19	LC	Atazanavir and degradation products	Seshachalam et al.	60
20	LC-MS	Genotoxic impurity in atazanavir sulphatedrug substance	Bhavani et al.	61

2.2 Literature survey on erlotinib and impurities

The literature survey revealed that some HPLC, spectroscopic methods and LC-MS/MS methods were developed for the quantification of erlotinib in biological matrices and different combination of drugs as per details given below table 2.2 [62-83]. From the literature review, it is noticed that none of the researchers attempted for the quantification of Ethyl 2-amino-4,5-bis(2-methoxyethoxy) benzoate and Ethyl 4,5-bis(2-methoxyethoxy) benzoate at ppm level in erlotinib hydrochloride by employing LC-MS technique.

Table 2.2: Literature review on different techniques for erlotinib and its impurities

S.No	Technique	Analytes	Author/s	Ref
1	RP-HPLC Assay method	Pharmaceutical formulations and Bulk drug	Chakravarthy et al.	62
2	RP-HPLC Assay method	Bulk and tablet dosage form	Ravi kumar et al.	63

S.No	Technique	Analytes	Author/s	Ref
3	RP-HPLC Assay method	Pharmaceutical formulation	Latha et al.	64
4	Stability indication assay method	Active pharmaceutical ingredient	Pujeri et al.	65
5	RP-HPLC method	Process-related impurities	Karunakara et al.	66
6	RP-HPLC method	Tablet dosage forms	Geetha et al.	67
7	HPLC-UV method	Gefitinib and erlotinib in human plasma	Faivre et al.	68
8	HPLC method	Erlotinib in Rat Plasma	Hou et al.	69
9	HPLC	Erlotinib protein binding studies	Soheila et al.	70
10	HPLC method	Erlotinib a tablet dosage form	Mohammed Ishaq et al.	71
11	HPLC-UV method	Vemurafenib and erlotinib in plasma from cancer patients	Zheng et al.	72
12	UPLC method	Erlotinib in pharmaceutical formulations	Naveen Kumar Reddy et al.	73
13	Spectrophotometric method	Pure and pharmaceutical dosage forms	Padmalatha et al.	74
14	Spectrofluorimetric method	Pure and pharmaceutical formulations	Rajesh et al.	75
15	Spectrofluorimetric method	Erlotinib in spiked human plasma	Mandal et al.	76
16	LC-MS/MS method	Erlotinib in spraguedawley rat serum, pharmacokinetic study	Raju et al.	77

S.No	Technique	Analytes	Author/s	Ref
17	LC-MS	Celecoxib, erlotinib, and its metabolite desmethyl-erlotinib in rat plasma with positive/negative ion-switching	Satheeshmanikandan et al.	78
18	LC-MS	Erlotinib, gefitinib, and imatinib in human plasma	Chahbouni et al.	79
19	LC-MS	Erlotinib (OSI-774) and OSI-420in human plasma	Andrea et al.	80
20	LC and LC-MS/MS method	Separation, identification, and characterization of degradation products	Mahajan et al.	81
21	LC-MS/MS method	Erlotinib in rat plasma sample	Zhang et al.	82
22	LC-MS	Method development and validation study for 3-ethynylaniline content in erlotinib	Narasimharao et al.	83

2.3 Literature survey on imatinib mesylate and its impurities

The various analytical methods for the quantification of imatinib mesylate and its impurities in various analytes were summarised in table 2.3 [84-102]. But no method was developed for the quantification of IMT-01 content in imatinib mesylate at low level quantification.

Table 2.3: Literature survey on different methods for imatinib mesylate and its impurities

S.No	Technique	Analytes	Author/s	Ref
1	Spectrometric method	Pure and tablet dosage form	Kumar Raja et al.	84

S.No	Technique	Analytes	Author/s	Ref
2	GC-MS	Genotoxic impurities in imatinib mesylate	Ramakrishna et al.	85
3	LC-MS/MS	Genotoxic impurity in imatinib mesylate	Vaibhav Bhatt et al.	86
4	LC-MS/MS	Potential genotoxic impurity in imatinib mesylate	Veera Reddy Arava et al.	87
5	UV spectroscopy	Bulk and solid dosage forms	Wajurkar et al.	88
6	RP-HPLC	Pure and pharmaceutical dosage form	Naga Sindhu et al.	89
7	RP-HPLC	Bulk drug and pharmaceutical dosage form	Ravi Shankar et al.	90
8	RP-HPLC	Pharmaceutical formulation	Arun Kumar Kuna et al.	91
9	GC-MS	Three potential genotoxic impurities in imatinib mesylate	Elżbieta et al.	92
10	X-RPD	Determination of two polymorphic forms	Esen Bellur Atici et al.	93
11	HPLC-Q-Orbitrap mass spectrometry	Human plasma	Mao-Wei Ni1 et al.	94
12	RP-HPLC	Tablets dosage form	Pratik Shah et al.	95
13	RP-HPLC	Pharmaceutical dosage form	P. Sandhya et al.	96
14	UV-spectrophotometric method	Bulk and tablet dosage forms	Suresha et al.	97

S.No	Technique	Analytes	Author/s	Ref
15	HPLC-UV detection	Quantification of imatinib mesylate and N-desmethyl imatinib	Ka Liong Tana et al.	98
16	RP-HPLC	Tablet dosage form	Arun Kumar Kuna et al.	99
17	RP-HPLC	Dosage forms	Shaik Munwar Pasha et al.	100
18	HPLC-UV detection	Imatinib in human plasma	Masatomo Miura et al.	101
19	LC-MS/MS	Human Plasma	Yunjing Zhang et al.	102

2.4 Literature survey on pantoprazole sodium and its impurities

Different analytical methods were developed for the quantification of pantoprazole and its impurities in different analytes were included in table 2.4 [103-120]. As per literature review, no analytical methods have been developed for the quantification of N-(4-hydroxyphenyl) acetamide, N-(4-(difluoromethoxy) phenyl) acetamide and 4-(difluoromethoxy)-2-nitroaniline at low level determination in pantoprazole.

Table 2.4: Literature survey on different methods using different techniques for pantoprazole and its impurities

S.No	Technique	Analytes	Author/s	Ref
1	RP-HPLC	Estimation of rabeprazole, pantoprazole, and itopride	Perumal et al.	103
2	UV spectrophotometric method	Bulk and tablet dosage form	Shinde Vaishali et al.	104
3	RP-HPLC	Bulk and in a synthetic mixture	B. Mahendar Amarnath et al.	105
4	HPLC	Pharmaceutical dosage form	Keyur B. Ahir et al.	106

S.No	Technique	Analytes	Author/s	Ref
5	Spectrophotometric method	Estimation of pantoprazole in bulk and pharmaceutical formulation	Pimpodkar et al.	107
6	NMR	Structural identification and characterization	Madhusudhan Reddy et al.	108
7	Spectrophotometric method	Estimation of pantoprazole and domperidone in pharmaceutical preparations	R.B. Kakde et al.	109
8	GC-MS	process related toxic impurities in pantoprazole sodium	V.V.S.S. Nanduri et al.	110
9	LC-MS/MS	Genotoxic impurity in pantoprazole	N. Venugopal et al.	111
10	UV-spectrometric	Estimation of cinitapride hydrogen tartrate & pantoprazole sodium in combined dosage form	M. Sravanthi et al.	112
11	LC-MS/MS	Estimation of Pantoprazole in human plasma samples	Balasekhara R. Challaaet al.	113
12	RP-HPLC	Pharmaceutical dosage forms and Human Plasma	Prasanna Reddy Battu et al.	114
13	LC-MS/MS	Pantoprazole in Rat Plasma	Xiangjun QIU et al.	115
14	LC	Pantoprazole in Human Plasma	Honggang Lou et al.	116

S.No	Technique	Analytes	Author/s	Ref
15	LC-MS/MS	Pantoprazole in Human Plasma	Osmair Peres et al.	117
16	HPLC	Pantoprazole and valsartan together in human plasma	Kocyigit-Kaymakcoglu et al.	118
17	HPLC	Etodolac and Pantoprazole in Rat Plasma	Abdelhameed et al.	119
18	Spectrometry	Determination of lansoprazole and pantoprazole sodium sesquihydrate	Azza A.M et al.	120

2.5 Literature survey on albendazole and impurities

Different analytical methods were developed for the quantification of albendazole and its impurities in different analytes were included in table 2.5 [121-130]. As per available literature review, no analytical methods have been developed for the quantification of 2-nitro-4-thio cyanato aniline and 2-nitro-4-propyl thio aniline in albendazole.

Table 2.5: Literature survey for albendazole and its impurities

S.No	Technique	Analyte	Author/s	Ref
1	HPLC	Pharmaceutical dosage forms	Y.S.R.Krishnaiah et al.	121
2	UV and HPLC	Oral suspension	Mariene et al.	122
3	HPLC	Bulk and synthetic mixture	Shreya et al.	123
4	UV	Tablet Preparations	Mahmood et al.	124
5	HPLC	Veterinary formulation	SPhatak et al.	125
6	HPLC	Albendazole and Praziquental	Sai Datri et al.	126
7	HPLC	Pharmaceutical dosage form	Patel Asmita et al.	127

S.No	Technique	Analyte	Author/s	Ref
8	HPLC	Tablet Dosage Form	Gandla et al.	128
9	UV	Bulk and Tablet Dosage Form	Ram S Wadje et al.	129
10	HPLC	Plasma	Z. Khalil et al.	130

2.6 Literature survey on quantification of genotoxic impurities by GC-MS and LC-MS method

In recent days, most of the researchers are using GC-MS and LC-MS techniques for the quantification of genotoxic impurities in different drug substances and pharmaceuticals in view of their high sensitivity. The related reviewed literature furnished in table 2.6 [131-150].

Table 2.6: Literature survey on different technique for genotoxic impurities

S.No	Analyte	Author/s	Ref
1	2-Mercapto Benzimidazole in Lansoprazole	Noor Shabana et al.	131
2	Genotoxic impurities in zolmitriptan	Vijay Bhaskar Reddy et al.	132
3	Genotoxic impurities in amlodipine	Srinivasa Rao et al.	133
4	Two genotoxic impurities in celecoxib	Vijay Bhaskar Reddy et al.	134
5	Genotoxic alkylation compounds	Wijk et al.	135
6	1,3-diisopropylurea in mometasonefuroateglucocortico steroid	Szekely et al.	136
7	(−)2-(2-amino-5-chlrophenyl)-4cyclopropyl-1,1,1-trifluro-3-butyn-2-ol genotoxic impurity in efavirenz	Nagadeep et al.	137
8	Chloroacetyl chloride a carcinogen in drug substances	Natarajan et al.	138
9	Organohalides in API's	Elder et al.	139
10	4-dimethylaminopyridine by design of experiment	Szekely et al.	140

S.No	Analyte	Author/s	Ref
11	Genotoxic impurity in active pharmaceutical ingredients.	Pennington et al.	141
12	Genotoxic impurities in drug substances	Jianguo An et al.	142
13	Genotoxic impurity in nevirapinedrug substance	Suneetha et al.	143
14	Three phenol impurities in ritonavir	Venugopal et al.	144
15	Genotoxic impurities in amlodipine drug substance	Srinivasa Rao et al.	145
16	Genotoxic impurities in Lopinavir and Ritonavir API.	Kakadiya et al.	146
17	Finisheddrug products by GC/MS	Wollein et al.	147
18	Six related impurities in darunavir drug substance	Vijaya Bhaskar Reddy et al.	148
19	Impurities in eslicarbazepine acetate API	Thamas et al.	149
20	Impurities in Emtricitabine API	Kakadiyaet al.	150

By overall literature survey reveals that several authors were investigated various drugs and pharmaceuticals for quantitative estimations of API and few of them attempted for the quantitative estimation of genotoxic impurities in trace level. None of the researchers worked on the quantification of genotoxic impurities at ppm level in respect of atazanavir sulphate, erlotinib hydrochloride, imatinib mesylate, pantoprazole sodium sesquihydrate and albendazole under investigation which is very essential for safety of human health.