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# Review on Determination of Preservative in Food Products and Pharmaceutical Products by Different Analytical Method

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## ABSTRACT:

Majority of instances of food spoilage can be attributed to the attack by pathogens (disease-causing microorganisms) such as bacteria and fungi, different methods that has been devised for preserving food for eliminate or reduce causative agent. Food preservative enhances human health by limiting growth of food borne pathogens and spoilage Micro-organisms. A substance which when added to food is capable of inhibiting, retarding, or arresting the process of fermentation, acidification or other decomposition of product. Consumption of food containing high levels of preservatives there are some harmful effects of preservatives. The describe methods were used for detection of different preservative and in various food stuffs and Pharmaceutical Formulation by different analytical techniques like UV-Visible, HPLC, GC, LCMS and Electrophoresis. Method of sample preparation which are used to prepare sample extraction methods; Ultrasonic assisted extraction, Supercritical fluid extraction, Pressurized liquid extraction, Stir bar sorption extraction and clean-up methods; Solid Phase Extraction, Solid Phase Micro-Extraction, Liquid Phase Micro-Extraction, Dispersive Liquid-Liquid Micro-Extraction, Matrix Solid Phase Dispersion. These methods are used to extract preservative from sample. Preservative Like Benzoic Acid, Sorbic Acid, Nitriles, Butylated hydroxy Toluene (BHT), Butylated hydroxy Anisole(BHA) Sulphur Including Sulphur dioxide, Sodium Benzoate, Methyl Paraben, Propylparaben.

**KEY WORDS:** UV-Visible, HPLC, GC, LCMS, Electrophoresis, Extraction Methods, Clean-up Methods

## 1. INTRODUCTION

**1.1 Preservatives**: Preservation are the compound used to prevent and retard the microbial spoilage of food or pharmaceutical products. Preservative as “a substance which added to food is capable of inhibiting, retarding or arresting the process of fermentation,acidification or other decomposition of product.

**1.2 Food Additives**:food additives are that substance not consumed as a food by itself and not used as a typical ingredient of the food or not it has nutritive value, the intention of addition is to food for a technological purpose in the manufacture, Treatement, preparation, processing packing, packing transport or holding of such food results, or may be reasonably expected to result(direct or indirectly) or otherwise affecting the characteristics of such food.Preservative are added to food and must be safe for consumption based on toxicological evaluation. Additives are used for the purpose of maintaining or improving the keeping quality, texture, consistency, appearance and other technological requirement.

Preservatives are classified into two classes. Class I and Class II preservatives.

**Class I preservatives**; salt which we use commonly, sugar, dextrose, glucose, spices, vinegar or acetic acid, honey, edible vegetable oils.

**Class II preservatives**; Benzoic acid, Sulphurous acid, Nitrates or Nitrites and Sodium and Potassium, Sorbic Acid

and its sodium, potassium and calcium salts, propionates of calcium or sodium, sodium potassium

Most commonly use preservatives are Benzoic acid, Sorbic acid, Butylated Hydroxy Anisole(BHA) and Butylated Hydroxy Toluene(BHT), Paraben, Sulphites, Nitrites and Nitrates.

**Benzoic acid**: Benzoic acid and sodium benzoate are used as food preservative and are most suitable for foods, fruit juices and soft drinks that are naturally in an acidic pH range. Their use as preservatives in toothpastes, mouthwashes, dentifrices, cosmetics and pharmaceuticals is regulated.

**Sorbic acid**: Sorbic acid is naturally occurring preservative the mostly use food preservative in the world and it makes the global food chain possible. USFDA considers sorbic acid to be safe for regular use, as it is not linked to cancer or other major health problems.

**Butylated Hydroxy Anisole(BHA) and Butylated Hydroxy Toluene(BHT):** Butylated Hydroxy Anisole(BHA) and Butylated Hydroxy Toluene(BHT) to foods like cereal and other dry goods to help their fats stay fresher longer. The international agency for research on cancer classifies BHA as possible human carcinogen. BHA and BHT are not used that are banned from foods in many countries Australia, Canada, New Zealand, Japan and Europe.

**Paraben:** Paraben are used for food preservation, prevention of mold, yeast and bacteria growth. Paraben are disrupted hormone function by mimicking oestrogen. More and more oestrogen can increase in breast cell growth of tumors, which is why paraben use has been linked to breast cancer and reproductive issues.

**Sulphites**: Sulphites also kill bacteria and fungus, giving foods a longer shelf life. And they slow the natural breakdown of vitamin C and A, lending to the claim that sulphites preserve nutrients. Sulphites reported a number of adverse clinical effects in sensitive human body, ranging from hypotension, dermatitis, flushing, dermatitis, diarrhea and abdominal pain diarrhea to life-threatening and dangerous anaphylactic and asthmatic reactions.

**Nitrites and Nitrates**: Nitrites and Nitrates they work by preventing or slowing down the growth of microorganism, like mould or bacteria. Nitrites and nitrates are used to preserve food, meat and cheeses. They can also be added to cured meat product to produce a pink color. In Various condition in our human body, nitrite damage cells and also convert into molecules that cause cancer. [1]

## 2. MATERIAL AND METHODS

### 2.1 Sample preparation methods:

#### 2.1.1Extraction Methods:

- Ultrasonic assisted extraction
- Supercritical fluid extraction
- Pressurized liquid extraction
- Stir bar sorption extraction

**Ultrasonic assisted extraction:** Sonication is the act of applying sound energy to agitate particles in a sample, for various purposes. Sonication relies on ultrasonic waves. probeinserted into a solvent mixture, and the probe then emits a series of high and low-pressure sound waves. Method consumes relatively long time and large volume of the solvents.

**Supercritical fluid extraction:** Extraction in the supercritical fluid extraction (SFE), supercritical fluids (usually is $co_2$), which can diffuse easily through solid materials and can therefore realize faster extraction because of their low viscosity and relatively high diffusivity, are adopted as extraction media to remove various kinds of substances from distinct types od solid matrices an improved SFE procedure. They added a co-solvent to $co_2$ to bring significant enhancement in the solubility and recovery. SFE eliminate organic solvent and provide cleaner extracts.

**Pressurized liquid extraction**: Pressurized liquid extraction also known as accelerated solvent extraction or pressurized fluid extraction, is one of the common extraction methods used to deal with solid sample that process is time and solvent saving, automatic extraction and high extraction efficiency. In the instrument pump, oven, extraction cell, solvent cell, nitrogen cylinder is there. First load sample then fill cell with solvent and heated and pressurized cell and hold sample at pressure and pump clean solvent then $N_2$ purging at last collect

**Stir bar sportive extraction:** stir bar sportive extraction (SBSE) was introduced as a solventless sample preparation method for the extraction of organic compounds from aqueous matrices. The method sorptive extraction is work on the solutes are extracted into a polymer coating on a magnetic stirring rod. A method based on the pressurized hot water extraction SBSE with a polydimethysiloxane(PDMS) stir bar and finally analyzed using thermal desorption-gas chromatography mass spectrophotometry. The combination od SBSE amd pressurized hot water extraction allowed the analytes to be preconcentratedand extracted from the aqueous

extract in a single step with minimal manipulation of the sample, and avoided risk of background contamination.

**2.1.2Clean-up Methods:**

Solid phase-extraction

Solid phase micro-extraction

Liquid phase micro-extraction

Dispersive liquid-liquid micro-extraction

Matrix solid phase dispersion

**Solid phase-extraction:** Liquid samples, SPE is directly used to treat real samples in general. for solid samples or oily samples, the analytes are extracted from the sample matrices using organic solvents. Organic solvent like methanol in advance, and then the SPE procedure is performed to the extract. SPE cartridge columns are activated before successive washing with different agent during a SPE process. Then the samples passed through cartridges at settled flow rates. The cartridges are then dried, and analytes are eluted from the cartridges.

**Solid phase micro-extraction:** solid phase micro-extraction, or SPME, is a solid phase extraction sampling technique that involves the use of a fiber coated with an extracting phase. that can be a liquid(polymer) or a solid(sorbent), which extracts different kinds of media. That is in liquid polymer or solid sorbent, which extracts different kinds of analytes including both volatile and non-volatile from different media. That is in liquid-phase or in gas-phase. The analyte quantity extracted with the fiber is proportional to its concentration in the sample as long as equilibrium is reached or, in short time pre-equilibrium, with convection or agitation.

**Liquid phase micro-extraction:** Liquid phase micro-extraction (LPME) technique has emerged from liquid-liquid extraction as an attempt to miniaturize and improve this technique. LPME is simple, rapid and inexpensive and it can be applied to a wide range of compounds. LPME method does not need special equipment and can decrease the consumption of organic solvent and matrix effects. This method is adapted to organic solvent whose densities are either lower or higher than that of water.

**Dispersive liquid-liquid microextraction**: Dispersive liquid-liquid micro-extraction (DLLME) is based on formation of tiny droplets of the extraction solvent in the sample solution by a rapid injection of a water-immiscible organic solvent(extractant) dissolved in a water-miscible organic solvent and the latter acts as a dispersing medium.

**Matrix solid phase dispersion:** MSPD is an SPE-based strategy in which a fine dispersion of th matrix is mixed with a sorbent material (C18, alumina,silica etc.) with a mortar and a pestle. Usually, solid samples are prepared for subsequent extraction and cleanup by a stepwise process that begins with the disruption of the sample.[2]

**Summary of sample preparation methods in brief:** crude samples to extraction and clean-up is a critical step in the process of sample preparation. And the applied sample treatment heavily depends on the kind of the matrix. For liquid samples, particulate matter was removed by filtration or centrifugation. The environment solid samples were usually homogenized, dried and sieved through a screen and then stored in dark at room temperature. food or cosmetic samples were stored in a refrigerator. For serum, the samples were processed with deproteinization. Among all the sample preparation methods, soxhelt, reflux, UAE, SFE, PLE and MSPD are preferred for the solid samples, while for the liquid samples, SBSE, SPE, SPME, LPME, and DLLME are preferred. Soxhelt and reflux extraction are old traditional methods which consumption of more amounts of organic solvents then other tech and extraction time.

High extraction efficiency can be obtained with SFE and PLE, but expensive instrument is required, when they are compared with UAE. MSPD different from the other techniques as we see. It is a manual technique, which combines sample then disruption and dispersal of the sample onto particles of a solid-phase support. Since SPME and SBSE are more selective methods and can be performed in solvent-free mode, the enrichment is clearly higher and compensates well for the lower recoveries. the column passing operation and the methods like SPE and PLE are to be complicated. multiple samples prepared simultaneously by SPE and PLE, the total time saved. The comparison of methods was summarized in this.

**3. CHROMATOGRAPHIC ANALYSIS:**

**3.1 Ultraviolet-visible spectrophotomethry:**(UV-Vis or UV/Vis) know as absorption spectroscopy in part of the ultraviolet and visible spectral regions. UV uses light in visible and adjacent ranges. In UV-Vis, beam with a wavelength between 180 and 1100 nm passes through solution in cuvette and absorbed light. The amount of light is absorbed by solution depends on the concentration, the path length of the light through the cuvette and how well the analyte the light absorbs at a certain wavelength. [17, 18]

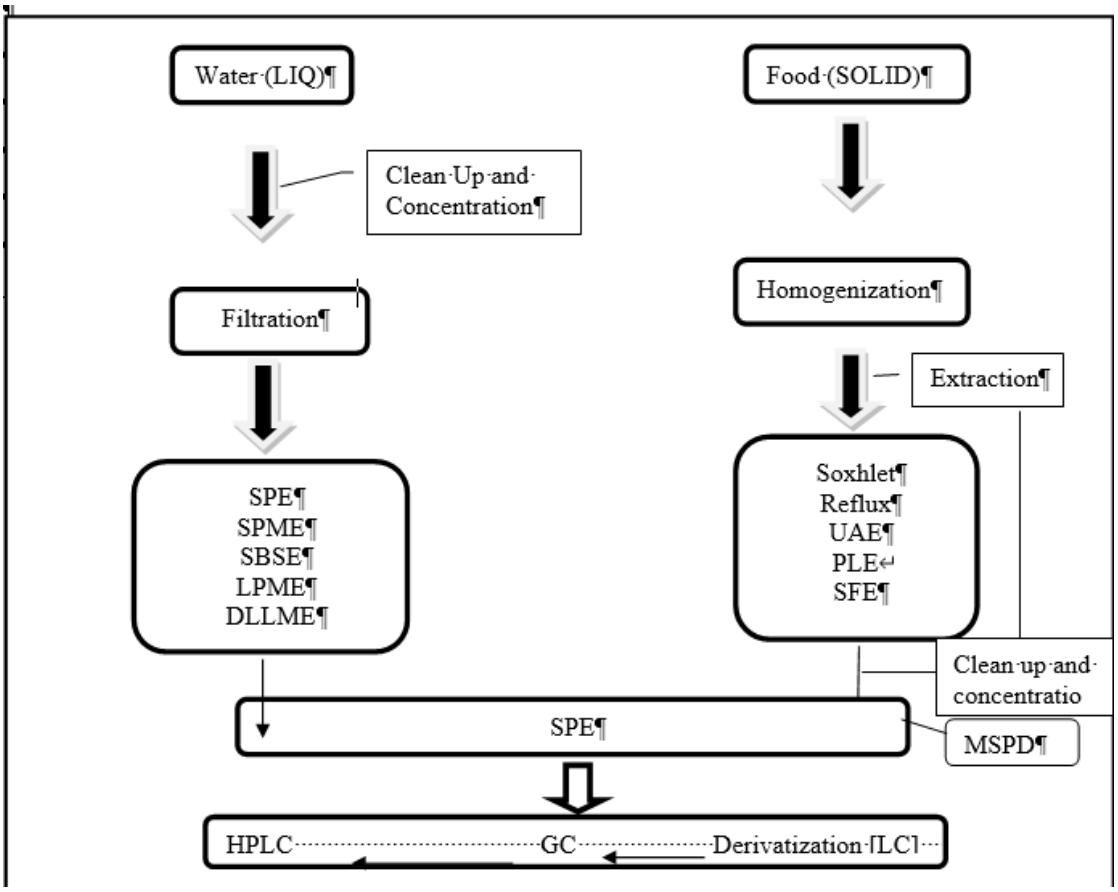


*Figure 1 comparison of methods*

*Table 1 Method of Extraction and Criteria*

| Method | Extraction time (min) | Solvent consumption (mL) | Mode of extraction | Operator skill | Equipment cost | Possibility of automation |
|---|---|---|---|---|---|---|
| Soxhelt | 5-24h | 100-200 | Sequential | Low | Low | Minimal |
| Reflux | 1-5h | 50-150 | Sequential | Low | Low | Minimal |
| UAE | May-60 | 20-100 | Sequential or Simultaneous | Low | Low | Minimal |
| SEF | Oct-30 | May-20 | Sequential | High | High | High |
| PLE | May-20 | 15-40 | Sequential | Moderate | High | High |
| SBSE | 20-70 | - | Sequential | Moderate | Low | Moderate |
| SPE | May-15 | 02-Oct | Parallel | Moderate | Moderate | Moderate to high |
| SPME | Oct-70 | - | Sequential | Moderate | Moderate | Moderate |
| LPME | Oct-70 | 0.01-1 | Sequential | High | Moderate | Moderate |
| DLLME | Oct-70 | 0.01-1 | Sequential | High | Moderate | Moderate |
| MSPD | May-20 | 02-Oct | Sequential | Low | Low | Minimal |

**3.2 High-Performance Thin Layer Chromatography:** HPTLC have similar approach and employ the same physical principles of TLC (absorption chromatography) i.e., the principle of separation is absorption. mobile phase solvent flows because of capillary action. The components move according to their affinities towards the absorbent occurs. [8]

**3.3 Gas chromatography - mass spectrometry**

**(GC-MS):** Gas chromatography-mass spectrometry (GC-MS) is an analytical method that combines the feature of gas-chromatography and mass spectrometry. The GC works on the principle that mixture will separate into individual substances when substances heated. gases are heated and carried through a column with an inert gas such as helium. As the separate substance emerge from the column opening, they flow into the MS. [13]

**3.4 High Performance Liquid Chromatography (HPLC):** High Performance Liquid Chromatography (HPLC) is a form of column chromatography that pumps a sample mixture or analyte in a solvent (mobile phase) at the high pressure through a column with chromatographic packing material (stationary-phase). The separation in HPLC based on the distribution. Distribution of the sample between a mobile phase and a stationary phase (packing material of the column). Depending on the chemical structure of the analyte, the molecules are retarded while passing the stationary-phase. The UV, VIS and PDA detectors are categorized by detectors according to absorbance. They provide good sensitivity for light-absorbing compounds. UV detector is very commonly used detector for HPLC analysis. [36,37]

**3.5 Capillary electrophoresis:** An analytical technique which separates ions based on their electrophoretic mobility with the use of voltage which applied. The electrophoretic mobility is dependent upon the charge of the molecule, viscosity, and the atom's radius. Capillary electrophoresis (CE) is a family of electrokinetic separation methods performed in submillimeter diameter capillaries and in micro- and nano-fluidic channels. Capillary electrophoresis (CE) refers to capillary zone electrophoresis (CZE), but other electrophoretic techniques including capillary gel electrophoresis (CGE) capillary isoelectric focusing (CIEF), capillary iso-tachophoresis and micellarelectrokineticchromagraphy (MEKC) belong also to this class of methods. In CE methods, migrateanalytes through electrolyte solutions under influence of electric field. Analytes separated according to ionic mobility and partitioning into an alternate phase by non-covalentinteractions.[4, 10]

**3.6 Ion-exchange chromatography:** in this chromatography analyte molecules retains on the column based on coulombic or ionic interactions. In this chromatography matric consists of positively charged and negatively charged ions. Molecules are interreact with electrostatic interactions with opposite charges at the stationary phase. The mobile phase, which contain the inorganic salt dissolved in a suitable solvent, is applied to the column. The mobile phase passes through the column, exchange between the H+ ions on the polymeric ion-exchange resin of the stationary phase and the cations of the salt in the mobile phase Ion exchange usually describes a process of purification of aqueous solution using solid polymeric ion exchange resins.[26]

**4. Analyst and Analytes with Sample preparation methods, Instrument analysis methods and Sample matrix**

*Table 2 Analyst and Analytes with Sample preparation methods, Instrument analysis methods and Sample matrix*

| Analyst | Description | | | |
|---|---|---|---|---|
| | Sample Preparation Methods | Instrument Analysis Methods | Analytes | Sample Matrix |
| Saad A, Raghad K and Duha S[3] | UAE | HPLC | Methylparaben, Propyl Paraben, Methylparaben Sodium, Propyl paraben sodium | Oral and Injection formulations |
| Bottoli C.B, Gutierrez-ponce | LPME | Capillary electrochromatography | Methylparaben, propyl paraben | Sweetenars |

| | | | | |
|---|---|---|---|---|
| M.J, [4] | | | | |
| Jankulovska M.s, markovska L.V, Ilievska B.P [5] | UAE | HPLC | Sodiumbenzoate, Potassium sorbate | Acidic food and beverages |
| Kamble R.M, Singh S.G, Singh S [6] | UAE | HPLC | Methylparaben, Propyl Paraben | Sucralfate suspension |
| Ozdemir A.[7] | SPME | HPLC-DAD | Sorbic acid | Cheese samples |
| Casoni D, Tuhutiu L.A, Sarbu C [8] | SPE | HPTLC | Methyl paraben, Ethyl paraben, Propyl paraben, Butylparaben | Suppositories, Pills, Weight Gain solution, Syrup |
| Kuok L, Hsieh Y [9] | UAE | Capillary electrochromatography | n-butyl p-hydroxybenzoate, methyl p-hydroxybenzoate, n-propyl p-hydroxybenzoate, Ethyl p-hydroxybenzoate | Solid food sample |
| Hou F, Deng X, Jiang X, Yu J [10] | DLLME | HPLC | Methyl paraben, Ethyl paraben, Propyl paraben, Butyl paraben | Soya suace, Tomato ketchup |
| Memon N, Bhanger I.M, Khuhawer M.Y [11] | UAE | HPLC and UV | Benzoic acid, Methyl Paraben, Ethyl paraben, Propyl paraben, Iso propyl paraben, Butyl paraben | Solid food sample and cosmetics like sampoo |
| Jaworska M, Szulinkska Z, Wink M [12] | Filteration and dilutions | Capillary electrophoresis | Benzyl alcohol, Phenol m-cresol chlorobutanolthimerosal CZE, Methylparaben, Propyl paraben PHBA | Syrup, Ointmnets |
| Styarini D, RamadhaninGtya D.P, Aristiawan Y, Aryana N [13] | SPME | GC-MS | Benzoic acid, Methyl paraben, n-Butyl paraben | Soy souce |
| Mazdeh F.Z, Moradi Z, | UAE | HPLC | Sodium benzoate, potassium sorbate, | Sports drinks |

| | | | | |
|---|---|---|---|---|
| Moghaddam Z [14] | | | caffeine, quiniline, sunset carmoisine | |
| Silva A.S, Cruz J.M, Garcia R.S, Losada P.P [15] | SPME | HPLC | Butylated hydroxyl toluene | Ketchup, soft cheese, gouda cheese, chocolate spread, pork meat, chicken breast meat, wheat flour, rice and honey |
| Shabir G.A, LOugh W.J, Arain S.A, Shar G.Q [16] | UAE | HPLC | Phenyl formic acid 2,4-hexadienic acid methyl 4-hydroxybenzoate propyl | Raw powederd preservative |
| Chua S.L, Teo S.S [17] | UAE | UV | Benzoic acid | Cola flavor soft drink |
| Reddy V.M, Aruna G, Parameswari A [18] | Separation | UV | Sodium benzoate, potassium sorbate | Pickles, Sauces, soft drinks, Fruit Juices, Jellies, Jams |
| Christinawaty, Damayanti s [19] | UAE | HPLC | BHA, BHT, Propyl Gallate TBHQ | Margarine |
| Khosrokhavar R, Sadeghzadeh N [20] | UAE | HPLC | Sodium benzoate, Pottasiumsorbate | Soft drik and extract samples |
| Altiokka G, Ergun B, Nafiz O, Hassan Y [21] | UAE | HPLC | Sodium benzoate | Ketchup, Jam, Soft Drink |
| Angelov T, Vlasenko A [22] | Filteration | HPLC | Methyl paraben, Ethyl paraben, Propyl Paraben, Butyl Paraben | Raw drugs |
| Zarad S.I, Nimkar N.R, Desai K.R [23] | Separation | HPLC | Benzoic acid | Tomato Kechup |
| | Separation | UV | Benzoic acid | Tomato Kechup |
| Zor S.D, Asc B [24] | UAE | HPLC | Potassium Sorbate, sodium benzoate | Lemon sauces |
| Chamandust S, Mehrasebi M.R [25] | SPME | Ion Chromatography | Nitrite, Nitrate | Milk sample |

| | | | | |
|---|---|---|---|---|
| Shah I, Petroczi A [26] | SPME | HPLC | Sorbic acid | Cheeze |
| Gomaa A.M, Amer M.E [27] | Filteration | HPLC | Sorbic acid, Benzoic acid | Juices |
| Jain A, Mathur P [28] | Distillation | Monier Williams method | Sulphites | Preserves, Dry fruits, Sugar, Bakery products |
| Hou F, Deng X, Jiang X and Jingng Y [29] | SPME<br>DLLME | UV | Methyl Paraben, Ethyl Paraben, Propyl Paraben, Butyl Paraben | Beverage Samples, Liquid milk products, Tomato ketchup, milk chocolate, chestnut Paste, Apple juice, Apple sauce, Soy sauce, Peanut butter, Beverage Samples Liquid |
| Badiadka N, Kenchaiah S [30] | Dilution | UV | Nitrite and Nitrate | Milk product |
| Bahremand N, Eskandari S [31] | UAE | HPLC | Sodium benzoate, potassium sorbate | Tomato ketchup |
| AmponsahD[32] | Separation | UV | Caffeine, Benzoic acid | Soft drink |
| Dong C, Mei Y, Chein L [33] | SPME | HPLC | Sorbic acid, benzoic acid | Milk chocolate, chestnut paste |
| Leuenberger U, Gauch R [34] | Clean up method | HPLC | Sorbic acid, Benzoic acid | Apple juice, Apple sauce, Soy sauce, peanut butter, beverage samples |
| Laura P, Giusepee D.L, Enrica Q[35] | Distillation | HPLC | Sulphite | Beer, Grapes fruit juices, Prunes |
| Kuang-Lung Kuo, You-ung Hsieh[36] | Extraction | HPLC | Sorbic acid, Benzoic acid | Plump Prserves,<br>Curd |
| Pylypiw H.M, Grether M.T [37] | Filteration | HPLC | Sodium benzoate, potassium sorbate | Liquid samples |

## 5. CONCLUSIONS:

Preservatives are most Widely used now a days. And recent studies have cautioned that Some preservatives may have harmful consequences. This have made the analysis of preservatives become necessary. Due to low level of

preservative found in sample matrices, it is necessary to undergo extraction and clean-up procedures prior to the determination step in order to improve detection limits.

all the sample preparation methods of extraction, SPE is the most widely use sample extraction and preconcentration method. In recent years, novel types of SPE using.LC and GC with different detectors are the dominating methods for the determination of preservatives. During the Lc determination Procedure, the large majority of works used conventional $C_{18}$ and $C_8$ columns, and the UV detection has been the most commonly used. Lc and GC is becoming more and more popular because it can offer better identification possibility and higher sensitivity. Although SPE is used commonly, it still needs a prior solvent extraction procedure for solid samples. MSDP used for solid samples and SPE becomes popular to treat liquid samples.

## 6. DISCUSSION:

In this review article sample preparation methods, soxhelt, Reflux, UAE, SFE, PLE and MSPD are prefferd for solid samples, while for the Liquid samples SBSE, SPE, SPME, LPME and DLLME are preferred. Then Analytical method was use to determine preservatives; HPLC, LC, Electrophoresis, GC, HPTLC etc.In that chromatographic analysis the mobile phase was important and column, sample matrix which type of sample is there for determination is important. Linearity and range should be in limit because it is harmfull in introduction part the Enumis thre and limits was given by authority of different nations for preservatives in food and other samples.

## 7. REFERENCES:


1. Food Safety and Standards Authority of India 2015. Manual of method of analysis of foods food additives

   https://old.fssai.gov.in/Portals/0/Pdf/Draft_Manuals/FOOD_ADDITVES.pdf Accessed 3 Feb 2020.

2. Cobzac SC, Gocan S. Sample preparation for high performance liquid chromatography: Recent progress, Journal of liquid chromatography and related technologies, 2011; 34: 1157-1267.

3. Saad A, Raghad K and Duha S. Determination of preservstivesparabens in oral and injection formulatations by HPLC, Asian Journal of Chemistry, 2013; 25(2):1123-1128.

4. Bottoli CB, Gutierrez-Ponce MJ, Aguiar VS, Aquino WM. Determination of parabens in sweeteners by capillary electrochromatography, Brazilian Journal of Pharmaceutical Science, 2011; 47: 779-785.

5. Jankulovska MS, Markovska LV, Lievska BP. High-performance liquid chromatography method for determination of preservatives in beverages, journal of agricultural,food and environmental sciences, 2016; 67: 18-25.

6. Kamble R.M, Singh S.G, Singh S. Simultaneous determination of preservative in sucralfate suspension using high performance liquid chromatography, E-journal of chemistry, 2011; 8(1): 340-346.

7. Ozdemir A, Sanli S, Sardogan S. Deternination of sorbic acid in cheese samples by rapid HPLC-DAD method, International journal of analytical chemistry, 2020; 1-4.

8. Casoni D, Tuhutiu L.A, Sarbu C. Simultaneous determination of parabens in pharmaceutical preparation using High-performance thin-layer chromatography and image analysis, journal of liquid chromatography & related technologies, 2011; 34: 805-816.

9. Kuok L, Hsieh Y. Determination of preservatives in food products by cyclodextrinmodified capillary electrophoresis with multiwavelength detection, Journal of chromatography A, 1997; 768: 334-341.

10. Hou F, Deng X, Jiang XY. Determination of parabens in beverage samples by dispersive liquid-liquid microextraction based on solidification on floating organic droplet, journal of chromatographic science,2014; 52: 1332-1338.

11. Memon N, Bhanger IM, Khuhawer MY. Determination of preservatives in cosmetics and food samples bymicellar liquid chromatography, Journal of separation science, 2005; 28: 635-638.

12. Jaworska M, Szulinska Z, Wink M. Application of a capillary electrophoresis method for simultaneous determination of preservatives in pharmaceutical formulation,journal of Separation science, 2005; 28: 137-143.

13. Styarini D, Ramadhaningtyas DP, Aristiawan Y, Aryana N. Simultaneous determination of benzoic acid and parabens in soy sauce by GC-MS, International Journal of advancement in engineering Technology, Management and Applied science,2017; 4: 103-111.

14. Mazdeh FZ, Moradi Z, Moghaddam Z, Khatoonabadi ZM, Aftabdari FE, Badaei P, Hajimahmoodi M. Determination of synthetic food colours, caffeine, sodium benzoate and potassium sorbate in sports drinks, Tropical journal of pharmaceutical research, 2016; 15(1): 183-188.

15. Silva AS, Cruz JM, Garcia RS, Losada PP. Determination of butylatedhydroxytoluene in food samples by high performance liquid chromatography with ultra detection and gas chromatography/mass spectrometry, Jornal of Aoac International, 2007; 90: 277-283.

16. Shabir GA, Lough WJ, Arain SA, Shar GQ. Method development and validation of preservatives(phenylformic acid, 2,4-hexadienoic acid, methyl 4-hydroxybenzoate and propyl 4-hydroxybenzoate) by HPLC, Journal of Liquid chromatography & related technologies, 2013; 29: 1223-1233.

17. Chua SL, Teo SS. Analysis of saccharin and benzoic acid in regular and diet cola-flavoured carbonate soft drinks, Internation Journal of food Science and nutrition, 2017; 2(4): 58-64.

18. Reddy VM, Aruna G, Parameswari A, Banu BH, Reddy PJ. Estimated daily intake and exposure of sodium benzoate and potassium sorbate through food products in school children of Tripura,India, International Journal of Pharmacy and Pharmaceutical sciences, 2015; 17: 129-133.

19. Christinawaty, Damayanti S. Simultaneous determination method of butylhydroxyanisole, butyl hydroxyl toluene, propyl gallate and tertiary butyl hydroquinone in margarine using high performance liquid chromatography, Asian Journal of pharmaceutical clinical research, 2015; 8(4): 209-211.

20. Khosrokhavar R, Sadeghzadeh N, Amini M, Ghazi-khansariM hajiaghaee R, EjtemaeiMehrsh. simultaneous determination of preservatives (sodium benzoate and Potassium sorbate) in soft drink and herbal extracts using high performance liquid chromatography (HPLC), Journal of Medicinal plants, 2010; 9(35): 80-87.

21. AltiokkaG, Ergun B, Nafiz O, Hassan Y. Validation reversed phase HPLC method for the analysis of the food additive,sodium benzoate, in soft drinks and jams, Journal of liquid chromatography & related technologies, 2007;30: 1125-1136.

22. Angelov T, Vlasenko A, Tashkov W. HPLC determination of pKa of parabens and investigation on their lipophilicity parameters, Journal of liquid chromatography &related technologies, 2008; 31: 188-197.

23. Zarad SI, NimkarNR, Desai KR, Solanki MS, Gandhi DM, Gandhi HM, Patel MS, Khimani AA, Saraliwala MN. Analytical Validation and comparative study of HPLC, spectrophotometric and titration method for determination of benzoic aid in food products, Asian Journal of chemistry, 2017; 29(7): 1565-1568.

24. Zor SD, Donmez OA, Kucukkaraca YD. Simultaneous determination of potassium sorbate, sodium benzoate, Quinoline Yellow and sunsetyellow in lemonades and lemon sauces by HPLC using experimental design, Journal of chromatographic science, 2016; 54(6): 952-957.

25. Chamadust S, Mehrasebi M.R, Kamali K, Solgi R, Taran J, Nazari F, Hosseini M.J. Simultaneous determination of nitrite and nitrate in milk samples by ion chromatography method and estimation of dietary intake, Internation journal of food properties, 2015; 1-25.

26. Shah I, Petroczi A, James RA, Naughton DP. Determination of nitite and nitrite content of dietary supplements using ion chromatography, Journal of Analytical &Bioanalytical techniques, 2013; 12: 1-7.

27. GommaAM,Amer ME, Attallah ER and Abo Elhassan AF. Validation of analytical method for determination of sorbic acid and benzoic acid in juices and carbonated beverages, Journal of Applied Sciences Research, 2013; 9(3): 1472-1476.

28. Jain A, Mathur P. Estimation of sulphite levels in food products available in Delhi,India" Journal of Nutrition & food sciences, 2016; 6: 1-12.

29. Hou F, Deng X, Jiang X, Jingang Y. Determination of paraben in beverage samples by dispersive liquid-liquid microextraction based on solidification of floating organic droplet, Journal of chromatographic science, 2013; 5: 1375-1378.

30. Badiadka N, Kenchaiah S. A spectrophotometric method for the determination of nitrite and Nitrate, Eurasian Journal Analytical chemistry, 2007; 4(2): 204-214.

31. Bahremand N,Eskandari S. Determination of potassium sorbate and sodium benzoate in “Doogh” by HPLC and comparison with spectrophotometry, International Journal of Bio-Inorganic Hybrid nanomaterials, 2013; 2(3): 429-435.
32. Amponsah D,” Determination of the amount of caffeine and benzoic acid in selected soft drinks” International Journal of Scientific &Enginnering Research, 2014; 5(6): 1375-1378.
33. Dong C, Mei Y, Chen L. Simultaneous determination of sorbic and benzoic acids in food dressing by headspace solid-phase microextracton and gas chromatography,Journal of chromatography A, 2006; 117: 109-114.
34. Leuenberger U, Gauch R, Baumgartner E. Determination of food preservatives and saccharin high performance liquid chromatography,journal of chromatography, 1979; 173: 343-346.
35. Pizzoferrato L, Lullo G, Quattrucci E. Determination of free, bound and total sulphites in foods by indirect photometry-HPLC, Journal of Food Chemistry, 1998; 63(2): 275-279.
36. Kuo K, Hsieh Y. Determination of preservatives in food products by cyclodextrin modified capillary electrophoresis with multiwavelength detection, Journal of chromatography A, 1997; 768: 334-341.
37. Pylypiw HM, Grether MT. Rapid high performance liquid chromatography method for the analysis of sodium benzoate and potassium sorbate in foods, Journal of chromatography A, 2000; 883: 299-304.
38. Saad B, Bari F, Salesh MI, Kamarudzaman A, Khairuddin M. Simultaneous determination of preservatives(benzoic acid, sorbic acid, methylparaben and propylparabne) in foodstuffs using high performance liquid chromatography A. 2007; 1073: 393-397.
39. Farahani H, Ganjali MR, Dinarvand R. Study on the performance of the headspace liquid phase micro extraction, gas chromatography-mass spectroscopy in the determination of sorbic and benzoic acids in soft drinks and environment water, Journal of Agricultural and food chemistry, 2009; 2633-2699.
40. Sangeetha S.,Mpharm Thesis,” Analytical method development for sodium benzoate and it’s application to soft drinks and fruit juices” Collage of Pharmacy shri Ramakrishna Institute of Paramedicalsciences,2016.