Research and Reviews: Journal of Pharmaceutical Quality Assurance

Method development and Validation – GCMS : Review

Oves Alaam*

Department of Pharmaceutics, Luqman College of Pharmacy, Gulbarga, India

Review Article

ABSTRACT

The intension of this paper is to survey and talk about the different strides required in GC technique advancement and approval. Gas chromatography is a delicate, precise, reproducible, quantitative and flexible instrument very much adjusted for the examination of complex blends. This system assumes a critical part in investigation of medications and pharmaceutical items. However the utilization of GC is constrained to unstable thermally stable mixes or the atoms that may experience derivatization responses to thermally stable items. Technique improvement and approval assume critical part in the revelation, advancement and produce of pharmaceuticals. Technique improvement is the way toward demonstrating that a systematic strategy is satisfactory for use to quantify the convergence of an API in a particular compound dose frame which permits streamlined strategies to be utilized to confirm that an examination method, precisely and reliably will convey a solid estimation of a dynamic fixing in a compound's readiness. The technique approval is crucial for explanatory strategy improvement and tried widely for specificity, linearity, exactness, accuracy, run, discovery confine, quantitation utmost, vigor and framework reasonableness.

INTRODUCTION

Gas chromatography is a remarkable and adaptable method. In its underlying phases of advancement it was connected to the investigation of gasses and vapours from extremely unstable segments. The work of Martin and Synge and after that James and Martin in gas–liquid chromatography (GLC) opened the entryway for an investigative method that has reformed compound partitions and examinations. As a logical apparatus, GC can be utilized for the immediate division and investigation of vaporous specimens, fluid arrangements, and unpredictable solids. On the off chance that the example to be examined is non-volatile, the strategies of derivatization or pyrolysis GC can be used. Gas chromatography is the logical procedure utilized for item recognizable proof (under extremely controlled conditions) and should be straightforwardly coupled to a mass spectrometer when data other than a near unique mark (program) is required, for example, positive distinguishing proof of tops on the chromatogram. 1The fundamental important of gas chromatography is that more noteworthy the partiality of the compound for the stationary stage, progressively the compound will be held by the section and longer it will be before it is eluted and recognized. Along these lines the heart of the gas chromatograph is the segment in which partition of the part happens, and to this must be included the source and control of the transporter gas course through the section, a mean of test presentation and a method for identification of the segments as they elute from the end of the segment. Since temperature will impact the instability of the analytes, the section is put in a thermostatically controlled stove[1-5]. Unlike most different sorts of chromatography, the versatile stage do not connect with atoms of analyte but rather just transport the analyte through the column3. Speedier gas chromatographic division is a for the most part useful alternative. Since the reduction time of investigation results in the expanded specimen throughput and therefore, the research facility operation expenses can be lessened altogether. Diminishment of investigation time can be accomplished by changing section parameters (shorter length, littler segment internal breadth, more slender film of stationary stage) or operational parameters (speedier temperature program rate, isothermal examination. Distinctive transporter gas, higher bearer gas stream rate or a mix of both methodologies can be applied[6-20].

GC Method Development

Strategies are created for new items when no official strategies are accessible. Substitute technique for existing (Non-Pharmacopoeial) items are to lessen the cost and time for better accuracy and toughness. At the point when interchange strategy proposed is planned to supplant the current methodology relative lab information including merit/negative marks are made accessible. 5Several stages are being considered for GC technique advancement like segment determination (stationary stage and measurements: segment id, length, and film thickness), bearer gas choice (Nitrogen, Helium, stream rate), temperature programing (Initial temperature, introductory hold, slope rate, last temperature, and last hold), injector tempreture and indicator temperature [21-26].

Steps required in Method advancement are.

1. Understanding the Physicochemical properties of test.
2. Selection of chromatographic conditions.
3. Developing the approach of examination.
4. Sample arrangement
5. Method improvement
6. Method approval

Understanding the physicochemical properties of sample

Gas chromatography is an interesting and adaptable strategy. In its underlying phases of advancement it was connected to the examination of gasses and vapors from exceptionally unpredictable segments. The blend to be isolated and broke down by GC might be either a gas, a fluid, or a strong in some instances.1Before starting the GC technique advancement, it is imperative to survey what is thought about the example. The objective of the examination ought to be characterized now and contemplations must be given to the quantity of tests to be dissected. 8Proper choice of the strategies relies on the way of the example (unpredictable or nonvolatile atom), its sub-atomic weight, dissolvability and softening point. 9As much as could reasonably be expected informations ought to be assembled about the examples including conglomeration state, test piece (analytes, grid, dissolvable), data on GC pertinent properties, for example, breaking point run, extremity, utilitarian gatherings, solvency, reactivity, solidness at room temperature within the sight of air. It ought to should be watched that, samples contain thermally or synthetically labile segments, forceful substances (corrosive, bases), water or nonvolatile deposits, does the specimen contain dangerous substances, any extraordinary taking care of required.10If the example to be investigated is nonvolatile, the procedures of derivatization or pyrolysis GC can be used. This last procedure is a change where in a nonvolatile example is pyrolyzed before it enters the column[27-32].

Selection of chromatographic conditions

The underlying decisions of section and supporting instrumentation affect the conceivable outcomes for, and extreme aftereffects of, division advancement. Control of section parameters (stationary stage, internal measurement, length, and film thickness) gives chromatographers control over segment proficiency, determination and speed of analysis.1 In gas chromatography, the elution request of analytes is administered by a few components, for example, idle vapor weights, solubilities in stationary stage, and inclinations for sub-atomic collaboration in the stationary stage. These impacts change with temperature and their coordinated impact at last decide the harmony appropriation of solute atoms between the portable and stationary phase [33-37].

Selection of Column

A segment is obviously, the beginning and focal bit of a chromatograph. A properly chose segment can create a decent chromatographic division which gives an exact and dependable examination. A shamefully utilized section can regularly create perplexity, deficient, and poor partitions which can prompt to results that are invalid or complex to translate. There are more than 10,000 aggravates that can be investigated by GC and more than 400 GC slim segments. It is a test for a section maker to give point by point segment choice rules to meet such a wide assortment of applications.12An enhanced chromatographic partition starts with the segment. The determination of the correct hairlike section for any application ought to be founded on four noteworthy variables which are stationary stage, segment inner breadth, film thickness, and segment length. The distinctions in the substance and physical properties of infused natural mixes and their communications with stationary stage are the premise of detachment process. At the point when quality of the analyte-stage collaborations varies essentially for two mixes, one is held longer than the other. To what extent they are held in the section (maintenance time) is a measure of these analyte-stage cooperations. Changing the substance components of the stationary stage adjusts its physical properties. Two aggravates that co-elute (don't discrete) on a specific stationary stage may isolate on another period of various chemistry [38-43].

Selection of Carrier Gas

A few dormant gasses can be utilized as the bearer gas or portable period of GC. Hydrogen, helium and nitrogen are all regular transporter gasses. Every transporter gas has its advantages and frameworks for which it is best suited. The selection of gas to be utilized as portable stage as a part of gas chromatography is affected by the accompanying necessities and considerations.

1. Inertness
2. Dryness
3. Freedom from oxygen
4. Safety
5. Cost
6. Availability

Optimization of Column oven temperature program

The section dwells in a broiler, and temperature, which significantly influences the adequacy of the chromatographic division, is a critical considers utilized controlling GC. As a rule, isothermal is not the best temperature mode for test partition; in such cases, a temperature program can be utilized. Most GC temperature program have beginning temperature, a slope (degree increment every moment) and a last temperature. Using a direct temperature program as a beginning stage if past investigation data is not accessible to use as aguide, the principal program advancement step is to attempt a basic, straight temperature program. To enhance the determination of prior eluting tops, diminish the underlying temperature or increment the underlying hold time. Diminishing the underlying temperature generally brings about the biggest determination change; however examination times are considerably expanded. The determination of pinnacles eluting amidst the chromatogram can be modified by change in slope rate. On the off chance that there is unreasonable pinnacle determination, the slope rate can be expanded to decrease determination and the examination time. On the off chance that there is lacking determination, diminish the slope rate; however there will be an expansion in the investigation time. Better determination of later eluting crests frequently happens while diminishing the slope rate. Another choice to change determination of tops amidst a chromatogram is to utilize a mid-slope hold. A mid incline hold is a few moment isothermal segment some place amid a temperature slope. Stop the temperature program not long after last pinnacle has eluted from the segment. On the off chance that section's isothermal temperature point of confinement is come to and pinnacles are as yet eluting, a last hold time is essential. Just utilize a last hold time if as far as possible is reached [44-50].

Optimization of Injector type, temperature & injection volume

Presentation of the specimen into GC framework is a basic stride in division. The reproducibility of the measure of test infused is essential to guarantee the reproducibility of results. A specimen can be infused physically into the framework or by utilizing an auto sampler framework. A noteworthy blunder in GC is poor infusion method. The injector temperature for detachment. The temperature of injector is utilized to quickly vaporize the fluid specimen into vaporous stage that can be conveyed to the section for detachment. In hairlike and miniaturized scale pressed gas chromatography (GC), there are four essential strategies for vaporizing an example and exchanging it onto the channel of the explanatory section: split, splitless, coordinate, and on-segment infusions. Of these, split and splitless infusions are the most normally utilized strategies. Part Injector was chosen for examination of test with high focus levels. In the split infusion mode, just a small amount of the vaporized example is exchanged onto the leader of the section. The rest of the vaporized example is expelled from the infusion port through the split vent line. Part infusions ought to be utilized just when test fixations are sufficiently high to permit a segment of the example to be disposed of amid the infusion procedure, while as yet keeping up an adequate grouping of analytes at the identifier to deliver a signal [51-55].

Optimization of detector type & detector temperature

An assortment of identifier is economically accessible to be utilized with GC, each having its own confinements and focal points. The most usually utilized locator as a part of GC is fire ionization finder. FID is normally utilized for natural mixes and utilized as a part of value control investigation of pharmaceutical mixes. Identifier temperatures and the relative stream rates of bearer gas, hydrogen and air into the locator are the key working parameters.13a arrangement of guidelines is characterized for assessment of indicator parameters, for example, float, clamor, affectability, straight range, dynamic range and so forth. The variety in identifier reaction with stream rate relies on upon whether the locator is fixation or mass stream subordinate. For fixation subordinate

locators (e.g., warm conductivity identifier, photograph ionization finder) a reduction in the stream rate does not influence the crest tallness, which remains roughly consistent.

However the pinnacle width, and thusly the pinnacle territory, increment. Conversely, for mass stream recognition frameworks (e.g., fire ionization identification, fire photometric discovery, and nitrogen phosphorus location) the reaction is contrarily relative to the maintenance time. In this manner, any change in chromatographic conditions which cause an adjustment in the maintenance time will likewise influence the pinnacle stature. It takes after that a lessening in the stream rate brings about decreased pinnacle statures, however the pinnacle region remains around constant [56-59].

Developing the approach for analysis

Two general ways to deal with GC technique advancement can be taken after, either begin without any preparation or scale a present strategy. The way that is taken relies on upon the status of the present strategy. Strategy interpretation yields a scaled rendition of the present technique. In the event that the present strategy meets the greater part of the diagnostic needs aside from speed, then interpretation is the most ideal approach (particularly if the investigation includes numerous segments). On the off chance that there are insufficiencies with the present strategy, It may be ideal to redevelop the technique without any preparation in orderto better meet the general logical requirements.14 Proper choice of the strategies relies on the way of the example (unpredictable or nonvolatile particle), its sub-atomic weight, dissolvability and liquefying point.9factors that influence gas chromatographic examination are segment temperature, transporter gas stream rate, infusion temperature, split proportion, finder temperature and test size.15All of these parameters are chosen on the premise of trials and took after by considering the framework appropriateness parameters. Run of the mill parameters of framework reasonableness are e.g. maintenance time ought to be more than 5 min, the hypothetical plates ought to be more than 2000, the following variable ought to be under 2, determination between 2 pinnacles ought to be more than 5, % R.S.D. of the zone of analyte tops in standard chromatograms ought not be more than 2.0 % like other [60-64].

Sample Preparation

The example that is infused into the gas chromatograph taking after specimen arrangement must be either a fluid or a gas, the analytes must be sufficiently unstable under the states of the bay and section to navigate the instrument, and, in a perfect world, the lattice impedances should likewise be unpredictable, so as not to defile the instrument or segment. Much of the time, fluid specimens must be broken up in an unstable natural dissolvable. The essential objective of test planning is to guarantee that these conditions are met, with extra objectives that the readiness be reproducible to meet quantitative examination necessities and straight forward to perform, if the investigation is to be performed routinely, as in quality certification and in other routine testing laboratories.1Before starting the GC technique improvement, it is vital to audit what is thought about the example. The objective of the examination ought to be characterized now and contemplations must be given to the quantity of tests to be broke down, accessible hardware, and so on. The way of the specimen (e.g. whether it is hydrophilic or hydrophorbic, whether it contains protolytic capacities, and so on) decides the best way to deal with strategy improvement. A few examples require a pre-treatment preceding examination as a result of the need to expel impedances or to focus test analytes. The specimen pre-treatment advancement can on occasion be more intricate than the division itself. The objectives of the partition ought to be indicated toward the start of the technique improvement. Additionally, before the example is infused amid the GC strategy improvement, the indicator ought to be chosen to be delicate to all specimen segments of intrigue. The last strategy ought to meet every one of the objectives that have been characterized toward the start of the technique advancement and when the technique for quantitative utilize is concluded it ought to be validated [65-68].

Method optimization

A few stages are included in strategy improvement and approval. On account of diagnostic systems like GC , these means may incorporate survey of data on tests to be dissected, meaning of partition objectives; confirmation of extraordinary strategy prerequisites, test pretreatment assuming any; locator choice and setting, division conditions streamlining, check for issues or unique technique necessities, recuperation of refined material, quantitative alignment and subjective strategy development.8The test conditions ought to be upgraded to get fancied detachments and affectability subsequent to getting proper divisions. This will be accomplished through arranged/systemic examination of parameters.16 During advancement one parameter is changed at once and set of conditions are disconnected instead of utilizing an experimentation approach [69- 72].

Method Validation

Approval is gotten from Latin from which signifies "solid ness". Approval is the quality or strongness of a strategy, process, and capacity of a gear to work and is demonstrated for its worthiness with affirmation and archived legitimately on the premise of logical data.17Validation of a systematic technique is the procedure by which it is set up by research facility ponders, that the execution attributes of the strategy meet the necessities for the expected explanatory application. Approval is required for any new or revised technique to guarantee that it is equipped for giving reproducible and dependable results, when utilized by various administrators utilizing a similar gear in the same or diverse research centers. The sort of approval program required depends totally on the specific technique and its proposed applications.13Results from strategy approval can be utilized to judge the quality, dependability and consistency of scientific results; it is an indispensable part of any great diagnostic practice. Utilization of gear that is inside particular, working effectively and satisfactorily aligned is crucial to the technique approval prepare. Diagnostic strategies should be approved or revalidated.

1. Prior to their presentation into routine utilize
2. Whenever the conditions change for which the technique has been approved
3. Whenever the technique is changed

Typical parameters recommended by FDA, USP, and ICH are as follow.18-20
1. Specificity
2. Linearity & Range
3. Precision
   - Method precision (Repeatability)
   - Intermediate precision (Reproducibility)
4. Accuracy (Recovery)
5. Solution stability
6. Limit of Detection (LOD)
7. Limit of Quantification (LOQ)
8. Robustness
9. System suitability

Specificity

Specificity of an explanatory technique as its capacity to evaluate unequivocally the analyte within the sight of segments, which might be required to be available. It can likewise be characterized as capacity of technique to quantify precisely an analyte within the sight of impedance, for example, engineered antecedents, excipients, enantiomers, and known (or likely) corruption items that might be relied upon to be available in the specimen matrix.

Linearity and range

The linearity of an expository strategy is its capacity (inside an offered range) to get test comes about, which are straightforwardly relative to the convergence of analyte in the specimen. A direct relationship ought to be assessed over the scope of the diagnostic method. It is shown straightforwardly on the medication substance by weakening of a standard stock arrangement of the medication item segments, utilizing the proposed method. Linearity is generally communicated as far as possible around the slant of the relapse line.20 For the foundation of linearity, least of five fixations are prescribed by ICH rule. The scope of an expository technique is the interim between the upper and lower levels that have been shown to be resolved with exactness, precision and linearity utilizing the method.

Precision

The exactness of a scientific strategy communicates the closeness of understanding (level of disperse) between a progression of estimations acquired from numerous inspecting of the same homogeneous example under the endorsed conditions. Accuracy might be considered at three levels: repeatability, middle exactness and reproducibility. It can likewise be characterized as level of understanding among individual test outcomes when strategy is connected over and again to numerous examining of a homogeneous example. 20The exactness of an explanatory methodology is generally communicated as the standard deviation or relative standard deviation of arrangement of estimations. Accuracy might be either the level of reproducibility or of the repeatability of the explanatory methodology under ordinary conditions. Middle of the road accuracy (otherwise called roughness) communicates inside labs varieties, as on various days, or with various examiners or gear inside same research

facility. Exactness of a logical strategy is controlled by testing an adequate number of aliquots of a homogeneous specimen to have the capacity to compute factually legitimate evaluations of standard deviation or relative standard deviation.

Accuracy (Recovery)

The exactness of an explanatory system communicates the closeness of assention between the esteem which is acknowledged either as an ordinary genuine esteem or an acknowledged reference esteem and the esteem found. It is dictated by applying the strategy to tests to which known measures of analyte have been included. These ought to be broke down against standard and clear answers for guarantee that no impedance exists. The exactness is then ascertained from the test comes about as a rate of the analyte recuperated by the test. It might frequently be communicated as the recuperation by the test of known, included measures of analyte [73-80].

Solution stability

Amid approval the solidness of guidelines and tests is built up under ordinary conditions, typical capacity conditions, and at times in the instrument to figure out whether unique stockpiling conditions are important, for example, refrigeration or assurance from light.

Limit of Detection (LOD)

Point of confinement of location (LOD) of an individual strategy is the most minimal measure of analyte in a specimen that can be distinguished however not really quantitated as a correct esteem. In scientific systems that display benchmark clamor, the LOD can be founded on a flag to-commotion (S/N) proportion (3:1), which is normally communicated as the grouping of analyte in the specimen. The flag to-commotion proportion is dictated by: s = H/h Where H = stature of the pinnacle comparing to the part. h = supreme estimation of the biggest clamor vacillation from the pattern of the chromatogram of a clear solution.

Limit of Quantification (LOQ):

The breaking point of Quantitation (LOQ) or Quantitation farthest point of an individual systematic technique is the most reduced measure of analyte in an example that can be quantitatively decided with reasonable exactness and precision. For scientific strategies, for example, HPLC that display benchmark clamor, the LOQ is for the most part evaluated from an assurance of S/N proportion (10:1) and is generally affirmed by infusing measures which give this S/N proportion and have a worthy percent relative standard deviation as well.

Robustness

is characterized as the measure of the capacity of a logical technique to stay unaffected by little yet think varieties in strategy parameters (e.g. pH, versatile stage organization, temperature and instrumental settings) and gives a sign of its unwavering quality amid ordinary utilization. Assurance of heartiness is an efficient procedure of shifting a parameter and measuring the impact on the strategy by checking framework appropriateness and additionally the examination of samples [81-84].

System Suitability:

Framework appropriateness tests are a basic piece of fluid chromatographic strategies. They are utilized to confirm that the discovery affectability, determination and reproducibility of the chromatographic framework are sufficient for the investigation to be finished. The tests depend on the idea that the gear, hardware, systematic operations and tests to be dissected constitute a fundamental framework that can be assessed accordingly. Variables, for example, the pinnacle determination, number of hypothetical plates, crest following and limit have been measured to decide the reasonableness of the utilized method [85-87].

CONCLUSION

Lately advancement of the investigative strategies for ID, immaculateness assessment and evaluation of medications has gotten a lot of consideration in the field of detachment science. This survey portrays GC technique advancement and approval by and large way. A general and extremely straightforward approach for the GC strategy advancement for the division of mixes was examined. Learning of the physiochemical properties of the essential compound is of most extreme significance before the any GC strategy improvement. Severa lsteps are being

considered for GC technique improvement like segment (stationary stage and measurements: section id, length, and film thickness), bearer gas choice (Nitrogen, Helium, stream rate), temperature programing (Initial temperature, starting hold, incline rate, last temperature, and last hold), injector determination, Injector temperature, identifier choice and locator temperature. Improved strategy is additionally should be approved with different parameters (e.g. specificity, exactness, precision, discovery constrain, linearity, and so on.) according to ICH rules.

REFERENCES

1. Ahamed MEH et al. Use of Bioinformatics Tools in Different Spheres of Life Sciences. J Data Mining Genomics Proteomics. 2014;5:158.
2. Rakesh M et al. Prediction of Genome and Protein Structures of Homo Sapiens Neanderthalensis Using NCBI Tools. J Data Mining Genomics Proteomics. 2014;R1:001.
3. Weier HUG. Bioinformatics for High Throughput Sequencing. J Data Mining Genomics Proteomics 2013; 4:e108.
4. Al-Haggar MMS et al. Bioinformatics in High Throughput Sequencing: Application in Evolving Genetic Diseases. J Data Mining Genomics Proteomics. 2013; 4:131.
5. Kondo Y and Miyazaki S. Protein Functional Site Prediction Using a Conservative Grade and a Proximate Grade. J Data Mining Genomics Proteomics. 2015;6:175.
6. Holmes RS and Cox LA. Bioinformatics and Evolution of Vertebrate Pancreatic Lipase and Related Proteins and Genes. J Data Mining in Genom Proteomics. 2012;3:111.
7. Sai YRKM et al. Bioinformatics Relevance in Biotechnology. J Proteomics Bioinform. 2011;4: 302-306.
8. Siva Kishore N and Mahaboobbi S. Statistics and Bioinformatics Ethnicity. J Proteomics Bioinform. 2011; 4: 294-301.
9. Nebel JC. Computational Intelligence in Bioinformatics. J Proteomics Bioinform. 2014; S9:e001.
10. Su J et al. Advances in Bioinformatics Tools for High-Throughput Sequencing Data of DNA Methylation. Hereditary Genet. 2012;1:107.
11. Dupont D et al. Assessing the Financial Impact of Reusing Electronic Health Records Data for Clinical Research: Results from the EHR4CR European Project. J Health Med Informat. 2016;7:235.
12. Waqas I et al. Treatment of Missing Values in Data Mining. J Comput Sci Syst Biol. 2016;9:051-053.
13. McCain P et al. Modulation of Stress in Coho Salmon, Oncorhynchus kisutch, using Feed Supplemented with Capsaicin. Poult Fish Wildl Sci. 2015;3:136.
14. Ali SH et al. A New Profile Learning Model for Recommendation System based on Machine Learning Technique. J Inform Tech Softw Eng. 2016;6:170.
15. Beresniak A et al. Assessing the Hair Colourings' Impact on Quality of Life. J Cosmo Trichol. 2015;1:103.
16. Mariam BG and Mariam TH. Application of Data Mining Techniques for Predicting CD4 Status of Patients on ART in Jimma and Bonga Hospitals, Ethiopia. J Health Med Informat. 2015;6:208.
17. Heidari A. Pharmacogenomics and Pharmacoproteomics Studies of Phosphodiesterase-5 PDE5 Inhibitors and Paclitaxel Albumin-stabilized Nanoparticles as Sandwiched Anti-cancer Nano Drugs between Two DNA/RNA Molecules of Human Cancer Cells. J Pharmacogenomics Pharmacoproteomics. 2006;7:e153.
18. Sharma V et al. Application of System Biology Tools for the Design of Improved Chinese Hamster Ovary Cell Expression Platforms. J Bioprocess Biotech. 2016;6:284.
19. Wright JC and Choudhary JS. DecoyPyrat: Fast Non-redundant Hybrid Decoy Sequence Generation for Large Scale Proteomics. J Proteomics Bioinform. 2016;9:176-180.

20. Bouwman FG et al. In Vitro, In Vivo Comparison of Cyclosporin A Induced Hepatic Protein Expression Profiles. J Clin Toxicol. 2016;6:299.
21. Vasko R et al. Comparative Serum Proteomic Analysis of Differentially Regulated Proteins in Patients with Rheumatoid Arthritis and Healthy Volunteers. J Arthritis. 2016;5:201.
22. Singla M et al. Differential Genomic Approach to Explore Phylogenetic Link. J Phylogen Evolution Biol. 2016;4:e118.
23. Elsebakhi E et al. Data Mining Risk Score Models for Big Biomedical and Healthcare Data. J Comput Sci Syst Biol. 2015;8:365-372.
24. Zhang J. A Complete List of Kernels Used in Support Vector Machines. Biochem Pharmacol Los Angel. 2015;4:195.
25. Shaukat K et al. Dengue Fever Prediction: A Data Mining Problem. J Data Mining Genomics Proteomics. 2015;6:181.
26. Gutch RS. Review Paper: Data Mining of Fungal Secondary Metabolites Using Genomics and Proteomics. J Data Mining Genomics Proteomics. 2015;6:178.
27. Shaukat K et al. Dengue Fever in Perspective of Clustering Algorithms. J Data Mining Genomics Proteomics. 2015;6:176.
28. Petrenko et al. Collaborative Complex Computing Environment Com-Com. J Comput Sci Syst Biol. 2015; 08:278-284.
29. Morris JA. Re-Discovering the Germ Theory of Disease: A Major Role for Proteomics. J Proteomics Bioinform. 2016;9:084-086.
30. Bo-Yeong C et al. Proteomics based Development of Biomarkers for Prion Diseases. J Proteomics Bioinform. 2016;9:087-100.
31. Gamberi T et al. Using Proteomics to Understand Abdominal Aortic Aneurysms: Where Are We? J Proteomics Bioinform. 2016;9:120-130.
32. Noronha MA et al. Developments in Cardiovascular Proteomics. J Proteomics Bioinform. 2016;9:144-150.
33. Li W et al. The Progress in Helicobacter Pylori High Risk Pathogenic Markers. J Hepatol Gastroint Dis. 2016; 2:128.
34. Sundari R. A Web Navigation Frame Work to Identify the Influence of Faculty on Students using Data mining Techniques. J Comput Sci Syst Biol. 2015;08:239-242.
35. Terence DM et al. Assessment of the Reliability of World Weather Online Forecasts for Kadoma Community. 2015;6:291.
36. Hailemariam T. Application of Data Mining Techniques to Predict Adult Mortality: The Case of Butajira Rural Health Program, Butajira, Ethiopia. J Health Med Informat. 2015;6:197.
37. Idemudia EC and Ferguson R. An Epistemological and Pattern Analysis of Empirical Data that Influences Emergency Loan Need Among Graduate Students. J Glob Econ. 2015;3:143.
38. Elsebakhi E et al. Novel Incremental Ranking Framework for Biomedical Data Analytics and Dimensionality Reduction: Big Data Challenges and Opportunities. J Comput Sci Syst Biol. 2015;8:203-214.
39. Wang KS et al. Statistical Modeling of MicroRNA Expression with Human Cancers. J Biom Biostat. 2015;6: 240.
40. El-Esawi MA and El-Ballat EM. Integrative Systems Biology: Addressing Biological Processes and Analysis of High-Throughput Bioinformatics Data. Biochem Physiol. 2016;5:e148.
41. Dubey A et al. Analysis of Caenorhabditis elegans via Bioinformatics Approaches Basis on their Precursors Statistics Values . Next Generat Sequenc & Applic. 2016;3:126.
42. Gill S et al. Serum Proteomic Analysis for the Identification of Biomarkers by Two-Dimensional Differential Gel Electrophoresis 2D-DIGE after Exposure to the Food-Processed Contaminant Furan. J Clin Toxicol. 2016;6:301.

43. Ruiz-Romero et al. Overlap Syndrome Systemic Sclerosis and Rheumatoid Arthritis with Achalasia: An Unusual Association. J Gastrointest Dig Syst. 2016;6:426.

44. Arpan A et al. Single Base Primer Extension Assay SNaPshot for Rapid Detection of Human Immunodeficiency Virus - 1 Drug Resistance Mutations. J Mol Biomark Diagn. 2016;7:271.

45. Shen Z et al. Identification of Host-Specific Genetic Markers within 16S rDNA Intervening Sequences of 73 Genera of Fecal Bacteria. J Data Mining Genomics Proteomics. 2016;7:186.

46. Mclean C et al. Improved Functional Enrichment Analysis of Biological Networks using Scalable Modularity Based Clustering. J Proteomics Bioinform. 2016;9:009-018.

47. Plummer E et al. A Comparison of Three Bioinformatics Pipelines for the Analysis of Preterm Gut Microbiota using 16S rRNA Gene Sequencing Data. J Proteomics Bioinform. 2015;8:283-291.

48. Lippolis R and De Angelis M. Proteomics and Human Diseases. J Proteomics Bioinform. 2016;9:063-074.

49. El Mowafy AM. Emerging Clues and Altered Metabolic Findings in Autism: Breakthroughs and Prospects from Omics Studies. Autism Open Access. 2016;6:166.

50. Chandramouli K. Marine Proteomics: Challenges and Opportunities. J Data Mining Genomics & Proteomics. 2016;7:e122.

51. Ahirwal MK et al. Adaptive filtering of EEG/ERP through noise cancellers using an improved PSO algorithm. Swarm and Evolutionary Computation. 2014;14:76-91.

52. Ahirwal MK et al. A new approach for utilisation of single ERP to control multiple commands in BCI. International Journal of Electronics Letters. 2014;2:166-171.

53. Roach BJ and Mathalon. Event-related EEG time-frequency analysis: an overview of measures and an analysis of early gamma band phase locking in schizophrenia. Schizophr Bull. 2008;34:907-926.

54. A Sano and Bakardjian H. Movement-related cortical evoked potentials using four-limb imagery. I J Neurosci. 2009;119:639-663.

55. Steven JL. An Introduction to the Event-Related Potential Technique. Cambridge, Mass: The MIT Press. 2005;pp388.

56. Vorobyov S and Cichocki A. Blind noise reduction for multisensory signals using ICA and subspace filtering, with application to EEG analysis. Biological Cybernetics. 2002;86: 293-303.

57. Wang Z et al. Single-trial evoked potential estimation using wavelets. Computers in Biology and Medicine. 2007;463-473.

58. Wastell DG. Statistical detection of individual evoked responses: an evaluation of Woody's adaptive filter. Electroencephalogr Clin Neurophysiol. 1977;42:835-839.

59. Ahirwal MK et al. Sub-band adaptive filtering method for electroencephalography/event related potential signal using nature inspired optimisation techniques. Science, Measurement & Technology, IET. 2015;9: 987-997.

60. Aydin S. Comparison of basic linear filters in extracting auditory evoked potentials. Turkish Journal of Electrical Engineering. 2008;16: 111-123.

61. Badcock NA et al. Validation of the Emotiv EPOC® EEG gaming system for measuring research quality auditory ERPs. PeerJ. 2013;1:38.

62. Behroozi M et al. EEG phase patterns reflect the representation of semantic categories of objects. Med and Biol Eng Comput. 2015;1-17.

63. Bonita JD et al. Time domain measures of inter-channel EEG correlation: a comparison of linear, nonparametric and nonlinear measures. Cogn. Neurodyn. 2014;8: 1-15.

64. Boutani H and Ohsuga M. Applicability of the Emotiv EEG Neuroheadset as a user-friendly input interface. Engineering in Medicine and Biology Society (EMBC), 35th Annual International Conference of the IEEE. 2013;1346-1349.

65. Croft RJ and Barry RJ. Removal of ocular artifact from the EEG: a review. Clinical Neurophysiology. 2000; 30:5-19.

66. Dixon WJ and Tukey WJ. Approximate behavior of the distribution of Winsorized t (Trimming/Winsorization 2). Technometrics. 1968;10:83-98.

67. Farquhar J and Hill NJ. Interactions between pre-processing and classification methods for event-related-potential classification. Neuroinform. 2013;11:175-1992.

68. Gajic D et al. Detection of epileptiform activity in EEG signals based on time-frequency and non-linear analysis. Front Comput Neurosci 2015;9:38.

69. Hu L et al. Taking into account latency, amplitude, and morphology: improved estimation of single-trial ERPs by wavelet filtering and multiple linear regression. J Neurophysiology. 2011;106:3216-3229.

70. Jervis BW et al. The removal of ocular artefacts from the electroencephalogram: a review. Medical and Biological Engineering and Computing. 1988;26: 2-12.

71. Jin J, et al. Optimized stimulus presentation patterns for an event-related potential EEG-based brain-computer interface. Medical and Biological Engineering and Computing. 2011; 49: 181-191.

72. Joyce CA, et al. Automatic removal of eye movement and blink artifacts from EEG data using blind component separation. Psychophysiology. 2004; 41: 313-325.

73. Linden DE. The P300: where in the brain is it produced and what does it tell us? The Neuroscientist. 2005; 11: 563-576.

74. Liu Y, et al. Implementation of SSVEP based BCI with Emotiv EPOC. Virtual Environments Human-Computer Interfaces and Measurement Systems (VECIMS), IEEE International Conference. 2012; 34-37.

75. Makeig S, et al. Independent component analysis of electroencephalographic data. Advances in neural information processing systems. 1996; 8: 145-151.

76. Marton LF et al. Technical signal processing with application in EEG channels correlation. Interdisciplinarity in Engineering International Conference "Petru Maior" University of Tirgu Mures, Romania. 2012.

77. Quiroga RQ and Garcia H. Single-trial event-related potentials with wavelet denoising. Clinical Neurophysiology. 2003; 114: 376-390.

78. Quiroga RQ, et al. On the performance of different synchronization measures in real data: a case study on EEG signals. Phys. Rev. E. 2002;65, 041903.

79. Ramírez-Cortes JM et al. P-300 Rhythm Detection Using ANFIS Algorithm and Wavelet Feature Extraction in EEG Signals. Proceedings of the World Congress on Engineering and Computer Science, (International Association of Engineers, San Francisco). 2010; 1: 963-968.

80. Xiang Chen et al. A homology-based pipeline for global prediction of post-translational modification sites. Scientific Reports 6, 2016; 25801.

81. Derui Wang and Jingyu Hou. Explore the hidden treasure in protein–protein interaction networks — An iterative model for predicting protein functions. J. Bioinform. Comput. Biol. 2015; 13.

82. Fahad Saeed et al. Introduction to the selected papers from the 7th International Conference on Bioinformatics and Computational Biology (BICoB 2015). Journal of Bioinformatics and Computational Biology. 2016; 14:03.

83. Lange K et al. Mendel: The Swiss army knife of genetic analysis programs. Bioinformatics. 2013;29: 1568-70.

84. MacHugh D.E. et al. Microsatellite DNA variation and the evolution, domestication and phylogeography of Taurine and Zebu Cattle (Bostaurus and Bos indicus). Genetics. 2015;146: 1071-86.

85. MacHugh D.E. et al. Genetic structure of seven European cattle breeds assessed using 20 microsatellite markers. Anim. Genet. 1928; 29: 333-40.

86. Martinez A.M. et al. Is the Murciano-Granadina a single goat breed? A molecular genetics approach. Arq. Bras. Med. Vet. Zootec. 2010; 62: 1191-8.

87. Maudet C. et al. Genetic diversity and assignment tests among seven French cattle breeds based on microsatellite DNA analysis. J. Anim. Sci. 2002; 80: 942-50.