Determination of antibiotic drug residues in milk and meat using different analytical methods: A review

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Abstract

Veterinary antibiotics are used in livestock production for control of animal diseases and as growth promoter. The repeated application of veterinary drugs for animals may result the occurrence of residues at various concentration levels in animal derived food products. Veterinary antibiotic residue is defined as small amounts of antibiotics, or its active metabolites which persists in animal derived food products after applying it in animals for different purposes. In particular antibiotic residues occur due to extensive application of antibiotics in veterinary services produce complications not only in dairy and meat industry but also have extensive public health consequences. Deleterious effects of drug residues residing in animal derived food products may induce carcinogenic and mutagenic effects and leads to the condition of antimicrobial resistance and antimicrobial allergy in the individuals who consume animal derived food products. Accordingly, it is important to effectively control antibiotic residues in animal derived food products. For that reason, regulatory authorities have enacted maximum residue limits (MRLs) for a number of veterinary drugs in different animal derived food products (milk, eggs and meat). Performing effective monitoring program requires specific, sensitive and reliable analytical methods that can identify all veterinary drug residues under regulated levels (MRL).

Introduction

Veterinary antibiotics are extensively applied for therapeutic and prophylactic of infections of different animals. By definition veterinary drugs are any substance applied or administered to any food-producing animals, such as meat or milk producing animals whether used for therapeutic, prophylactic, or diagnostic purposes (1). Veterinary drugs can be divided into six classes such as: antimicrobials anti-parasites, anti-inflammatory drugs, tranquillizers, drugs with growth promotional effect and others (2).

Antimicrobials are the dominant class of veterinary drugs used after 1950s to treat bacterial infectious diseases in animals. Extensive and unrestricted use of veterinary antibiotics can facilitate the occurrence of veterinary antibiotic residues in animal derived food products like milk, meat and eggs. Existence of veterinary antibiotic residues in animal products milk and meat may cause allergies in humans, and in extensive and long run may facilitate the development of resistant pathogens. The existence of resistant bacterial strains produces severe health consequences on humans health (3). Therefore, it is important to effectively control antibiotic residues in animal derived food products and regulatory authorities have validated maximum residue limits MRLs for different veterinary drugs in eggs, milk and meat. National residue monitoring programs to control veterinary drug residues in different animal derived food products including meat and milk are compulsory in all nations. Higher amounts of veterinary antibiotic residues in animal product supplies higher than the MRLs are illegal. Conduct effective veterinary antibiotic monitoring program requires specific, sensitive and reliable analytical methods that can detect all antibiotic drug residues below regulated levels (4). There are various analytical methods which are used to determine antibiotic residues in animal derived food products, some of the methods include: microbiological, chromatographic, immunochemical, and biosensor tests (2).

Full Text

Antimicrobial drug residues

Antimicrobial residues are defined as all active ingredients or its metabolites of those drugs or degradation products that remain in animal derived food products (5). The use of veterinary antibiotics for food producing animals may cause the existence of residues in foodstuffs of animal origin like meat and milk (6).

Risk factors for antibiotic residue occurrence

Most of the time livestock producers treat entire groups of livestock animals. This activity unintentionally and unnecessarily can expose healthy animals to antimicrobials. Additionally, many livestock producers administer sub therapeutic doses of veterinary antibiotics to treat infectious diseases and this will cause to antibiotic residue entering the human food chain (7). Animal fecal recycling, where the drug residues can excreted in the feces of treated animals, which will contaminate the feed of untreated animals, this can also be the cause of occurrence of veterinary antibiotic residues (7).

Improper withdrawal time

Withdrawal time is the time for the residue of toxicological concern to reach a safe level of drug concentration. The withdrawal time can varied for different veterinary drug products depending on different conditions such as: the type of drug, dosage form and route of drug administration. Withdrawal time can also be defined as the interval between the last administration veterinary drug to the animals of the drug under normal condition of used and the time when treated animal can be slaughtered for the production of safe foodstuffs (8). Therefore, fail to wait for withdrawal period causes occurrence of residue in food of animal origin such as meat and milk, which is used for human consumption (7).

Safety evaluation of veterinary antibiotic residues

Acceptable daily intake

By definition acceptable daily intake for a given drug is the amount of a drug that can be ingested everyday over a lifetime without appreciable health risk on the consumer (9). Acceptable daily intake also defined as a maximum amount of drug residues or chemicals, which can be consumed everyday by the most sensitive classes in the population with any out ward effects on their health (10).

The acceptable daily intake can be calculated by using a safety or uncertainty factor, which is commonly 100, to the no observed adverse effect level (NOAEL) obtained from the most sensitive test species. The 100-fold safety factor is based on the need to take into account both the variations in species and variations in toxicokinetics and toxicodynamics (11).

ADI = Long-term NOAEL (lowest value)/100 *Eq. 1*

Maximum residue limits (MRL)

The term maximum limit for residues of veterinary antibiotics or drugs is the maximum concentration of veterinary drug residues resulting from the use of veterinary drugs to be legally permitted or which is recognized as acceptable in animal food products. The concentration of drug residue can be expressed in milligrams/micrograms per kilogram of the commodity (or milligrams/micrograms per liter in the case of a liquid commodity) or ppm/ppb (12). A residue at or below the stated MRL is considered safe when animal derived food at that level is consumed daily for a lifetime (Table 1). The MRLs are specified for several animal derived food products (different edible tissues and other food commodities). When veterinary drugs are used according to the period of treatment and the withholding period specified before slaughter or milking, the concentration of drug residues should be at levels that will not cause adverse effect on the health of the consumer. Therefore animals are suitable for food production if the amounts of veterinary antibiotic residues in animal food products are below levels that could cause a health risk for consumers (13).

Now days regulatory body have been established for veterinary drugs used in food producing animals for regular monitoring of veterinary drug residues in livestock products. The regulatory laws can help the government policies in managing animal derived food safety, prevention, and control of food safety incidents (12).

Table 1
Maximum antibiotic drug residue limits for commonly used antimicrobials in food staffs of animal derived.

Antimicrobial	Muscle (µg/kg)	Liver (µg/kg)	Kidney (µg/kg)	Fat (µg/kg)	Cow milk (µg/L)
Amoxicillin	50	50	50	50	4
Benzyl penicillin	50	50	50	50	-
Chlortetracycline/oxytetracycline/ tetracycline	200	600	1200	-	100
Gentamycin	100	2000	5000	100	200
Streptomycin/dihydrostreptomycin	600	600	1000	600	200
Erythromycin	-	-	-	-	-
Neomycin	500	500	1000	500	1500
Sulfadimidine	-	-	-	-	25
Tilmicosin	100	1000	300	100	-
Tylosin	100	100	100	100	-

Impact of antimicrobial residues

The incidence of veterinary antibiotic residues in animal derived food produces a significant health risk on the health of consumers because of the emerging of microbial resistance noticed in recent years (14). Extensive use of antibiotics might increase the risk of an adverse effect of residues on the customer and the occurrence of antibiotic resistance as well as hypersensitivity reactions on consumers (7). Therefore, ingenuity use of veterinary antibiotics in the manner of preventing animal feed and food contamination is required (10).

Antimicrobial resistance

The emergence of antimicrobial resistance has been observed due to different factors. Some of the factors include repeated use and exposure to sub lethal dose of antimicrobials (14). In addition, the application of animal manure for soil fertilization can be contemplate contributor for environmental contamination and transmission of antimicrobial drug residues through animal feces. Currently development of antimicrobial resistant bacterial genes frequently described owing to the overuse of veterinary antimicrobials all over the world. The utilization of veterinary antimicrobials in food producing animals causes selection for bacterial resistant to antimicrobials. When these antibiotics administered to humans causes poor response to treatment during illness (15).

The extent of veterinary antibiotic residue in Ethiopia

In most African countries, veterinary antibiotics maybe applied indiscriminately for the treatment of infectious diseases or they may be used as feed additives for domestic animals. Current threat of antimicrobial residue is a major challenges for public health. These challenge faced the human population worldwide including Africa (16). These veterinary antibiotic residues are escalating rapidly, disregarding of topographical, biological, or legitimate variations among countries (16, 17).

A study conducted in Ethiopia for determination of oxytetracycline and penicillin G residues in milk samples from farms (Nazareth dairy farms). From the total 400 milk samples, 48 milk samples were found to contain oxytetracycline and penicillin G residues.

Another study was also conducted in 2007, a study conducted in Ethiopia specify the percentage of tetracycline residue levels in beef. Among the meat samples collected from the three sampling sites (Addis Ababa, Debre Zeit and Nazareth slaughterhouses) 93.8%, 37.5% and 82.1% tested positive for oxytetracycline residues respectively (18).

Codex and food safety system in Ethiopia

By definition the Codex Alimentarius commission is the international body which is responsible for the execution of the joint FAO/WHO food standards program (19). It was established in 1962 by FAO and WHO, the program is aimed at safeguarding the health of customers and facilitates international trade in foods (20).

The Ethiopian National Codex Committee (NCC) was established under the auspices of the Quality and Standards Authority of Ethiopia (QSAE) in 2003 (19). NCC member organizations are Addis Ababa University, ministry of health, ministry of agriculture, ministry of trade and ministry of industry, Ethiopian public health institute and (21) consumers association and Ethiopian chamber of commerce and QSAE (22).

The principal responsibilities of the national codex committee are endorsement of recommend Codex standards as Ethiopian standards, represent the country's interest on selected international Codex meetings, detect priority areas on food safety and expand fundable projects and conduct national awareness program on food safety and codex standards (21).

Analysis of antibiotic drug residues

Sample pre-treatment

Occurrence of antibiotic residues can varied within a single organ and it is a main factor to contemplate before sample preparation. For instance, residue differences can occur in the kidney between the medulla and the cortex (23). Accordingly, it is important to take a characteristic aliquot of the biological sample. This may need removal of some portions throughout the composite sample to get a representative sample (24). Homogenization with a blender is often important to get a homogenous biological sample. Liquid biological samples like milk are generally easier to process than solid samples and antibiotic residues are more homogenously distributed throughout (24).

Sample extraction techniques

Drug residue extraction is the removing of an active agent (antibiotic residue) from solid (animal tissues and organs) or liquid mixture (from milk) with extraction solvent. Extraction solvent used is not or only partially miscible with the solid or the liquid (25). Considerable contact between analyte and the extraction solvent leads the analyte transferred from the solid or liquid mixture into the extraction solvent (25). Following exhaustive mixing, the two phases can isolated either by gravity or centrifugal forces (26).

The major goal of sample extraction process is to get a suitable sample for analytical instruments, commonly for chromatographic analysis, that will not contaminate the analytical instrument. The method of biological sample preparation and extraction technique selected is generally dictated by the analytical methods accessible and the physical characteristics of the residues in the process of investigation (24).

Solvent extraction technique

In solvent extraction method, the biological sample (most of the time meat) are assorted with the selected extraction medium or solvent. The solvent helps to dissolve veterinary drug residues and other biological extractives. Extractive solvent also promote deproteinsation of biological samples (22). Most of the time organic extraction solvents are distinctly important in veterinary drug residue analysis because they enable extraction of protein associated veterinary drugs from biological samples. Factors to be

considered during selecting of an extraction solvent are thermodynamic properties of extraction solvent and its ability to interact with the analyte (26).

Some organic solvents such as acetonitrile, methanol and ethanol are water miscible and frequently applicable in veterinary drug residue extraction. This is due to the polar behavior of majority veterinary antibiotic drugs. Proteins from biological samples are generally not soluble in organic solvents. Therefore organic solvents help to precipitate proteins, hence veterinary drug residues can be left from protein binding sites (27).

For polar antibiotic residues, aqueous extraction solvents can be applied. Assorting the pH of an extraction solvent can increase the polarity of extraction solvent. Therefore it may have greater capacity for solubilizing polar veterinary antibiotic residues. mineral acids were utilized for the extraction of tetracyclines residues, since this drug is not acid labile (13).

Liquid-liquid extraction

One of the most useful residue extraction techniques from biological matrix is liquid-liquid extraction (28). It is a technique applied for isolation and extraction of analyte from a mixture using two immiscible extraction solvents (28). The concept “like dissolves like” works well in LLE method of antibiotic residue separation from biological matrix. The capacity to isolate analytes from a mixture using this technique depends upon how differently the compounds in the sample mixture partitioning themselves between the two immiscible phases (solvents). scrupulous partitioning of the analyte of interest (antibiotic residue) into one of two immiscible or partially miscible phases occurs by appropriate selection of extraction solvent (26).

Clean-up methods

Most biological sample matrices contain endogenous compounds that have negative impact on detection of antibiotic residues, so after extraction, different clean up techniques can be used to remove interferences. Interference is defined as any component of biological samples that can prevent or hinder the process of determining the analyte or drug residues (9).

Dispersive-solid phase extraction (DSPE)

It is a clean-up method wich require mixing of sorbent with sample, which has been pre-extracted with proper extraction technique. Proper sorbent adsorbs matrix co-extractives onto its surface, leaving analytes of interest in the solvent (29). In the process magnesium sulfate ($MgSO_4$) can be added to get extra clean-up by withdrawing residual water and some other components *via* chelation (29). Subsequently, the mixture can be centrifuged and the resulting supernatant or filtrate can be analyzed directly or can be subjected to a concentration and solvent exchange step (30). DSPE is an extremely rapid, simple and cheap process that provides high recovery and reproducibility for many liquid chromatography and gas chromatography-amenable analytes (30).

Immunoaffinity column chromatography

Now days, immunochemical methods are mostly applied for the separation of antibiotic residues from biological. These method gives high specificity, sensitivity, and high sample throughput (31). In this technique, antibodies against the analytes or residue of interest will be immobilized on the surface of solid sorbent support that is packed into syringe barrel. For developing of immunoaffinity column method, different parameters may be adjusted to attain ideal separations. Some of the parameters include, the properties of the sorbent, the integrating mechanism for immobilization of antibody on to the surface of sorbent and the property of the antibody. Optimal sample loading, proper cleaning and elution techniques should be determined after preparation of the immunoaffinity column. The effectiveness of the technique depends on the capacity of the antibody to tie up the residue or analyte of interest. For better antibody-antigen interaction it is necessary to work under optimal conditions, which are as close as possible to physiological conditions. Such characteristics limits the application of this technique to polar veterinary antibiotics. Maximal heat, pH and organic extracting solvent content may cause denaturation of antibody on the solid support. Throughout sample loading, some conditions must behave to the establishment of the antigen and antibody complex. Formed antigen antibody complex should not be overblown by washing solvents and elution conditions which is essential for dissociation of the antigen-antibody complex (32). Additionally, the dissociation of antibody/antigen complex must ideally be reversible. Therefore the antigen-antibody complex can comfortably reformed, which helps re-use immunoaffinity column. Hou *et al* used Immunoaffinity Chromatography Cleanup for Simultaneous Analysis of Avermectins in Bovine Tissues by LC-MS-MS method (33).

Screening methods

Several tests have been described for the screening of antimicrobial residues in various biological samples. Bio based screening methods were applied for the detection of antimicrobials in animal derived food products have been reviewed (34–36). The most frequently used bio-based screening methods for antimicrobial are microbiological inhibition assays, immunoassays and biosensor tests (37).

In the process of screening methods, compliant samples are accepted and those suspected non-compliant samples have to be re-checked and confirmed using other confirmatory methods. A scheme of the typical screening analysis procedure is shown in Fig. 1. In antibiotic residue determination, high throughput methods with low cost and able to identify an analyte or class of analytes at the level of interest are needed (38). In the event, antibiotics which have a maximum residue limit, the screening analytical method, should be able to identify the residue under the maximum limit. The screening analytical methods must also avoid false negative results because they will be considered as compliant samples and will not be analyzed or determined by confirmatory analytical methods. Additionally, screening analytical method must not give an excessive number of false non-compliant samples that will be later confirmed as compliant, after extra cost and time involved (39).

Microbiological inhibition assays

Microbiological inhibition assays is one of the most widely used screening analytical method. The principle of this technique is based on a reaction between bacteria and antimicrobials which are present in biological samples. Various biological tests were expanded to screen various antibiotic residues from animal derived food products (34). There are two most common formats for microbiological inhibition assays such as the tube and plate tests (40).

The tube test of microbiological assay comprises of a growth medium inoculated with a bacterium, supplemented with a pH or redox indicator. Then biological samples are added to the tube, if there is no particular antimicrobials are present in the biological sample, the bacteria begin to grow and produce acid, which will cause a detectable colour change. Conversely, if antimicrobials are present in the biological sample that inhibit bacterial growth, no colour change will occur in the tube (41).

The plate microbiological test comprises of a layer of nutrient agar inoculated with bacteria and the biological samples are brought onto the surface. If there is no specific antimicrobials are present in the biological sample, the bacteria begin to grow throughout the plate. If a specific antibiotic is present in the biological sample (meat or milk), no bacterial growth will takes place on the sample, that can be observed from the bacterial free inhibition zone (40).

Now days, microbiological inhibition tests are accessible as kits with a high sample throughput (high productivity). Microbiological tests need restricted laboratory capacity to make certain reproducible situation of application. Microbiological tests are extensively used to perform antibiotics residue control (42).

The advantages of microbiological inhibition assays, compared to immunoassays and instrumental analytical methods, microbiological tests can detect any antibiotic residues that shows antibacterial activity (43). Moreover, these tests have the potential to cover the entire antibiotic spectrum within a single test (42). The limitation of these techniques are their lack of selectivity, especially the tube microbiological inhibition test, relatively high detection limits and the long bacterial incubation time. Consequently, microbiological inhibition assays are not suitable for detection of banned antibiotic compounds like chloramphenicol (40).

Immunological techniques

Antigen and antibody interaction has been used for many years to identify a wide variety of food constituents including substances responsible for adulterations and contaminations (44). The interaction of antigen and antibody is very specific and useful for the detection of veterinary drug residues in animal derived food products. The most widely used methods comprises of enzyme-linked-immunosorbent assay (ELISA). The detection system ELISA is usually based on enzyme-labelled reagents. There are various formats for the enzyme-linked-immunosorbent assay (ELISA) technique. The first form of ELISA technique is sandwich ELISA tests, in this technique a primary antibody is bound to the plate well. Then antigen of the sample extract added to the well complexes with the bound antibody and remains bound to the plate after washing. Then, a second antibody, which is labelled with an enzyme such as peroxidase,

is added to the well followed by additional washing of the well. The quantity of conjugate bound to the plate is detected after incubation with a specific substrate (23). Then colour is developed during incubation and measured with a microplate reader, which is proportional to the amount of analyte in the sample (23).

The second type of ELISA technique is direct competitive ELISA tests, in this technique a primary antibody is coated onto the plate wells and incubated with the sample extract containing the antigens. After the equilibrium is reached, an enzyme-labelled antigen can be added. This conjugate will bind to the free binding sites of the primary antibody. Thus, the more antigen in the sample (biological sample in this case), the lower amount of enzyme-labelled antigen bound will formed. Then appropriate specific substrate is added and the plate is incubated for colour development. In this case, there is an inverse relationship between the colour developed and the concentration of the analyte in the sample (45).

ELISA technique is extensively used and specific test for screening of veterinary antimicrobial residues in animal derived food products. The Competitive ELISA technique is frequently applied for quantitative determination of antibiotic residues in meat (45, 46).

Biosensors

Biosensor is one of screen analytical method for veterinary drug residue analysis. Various types of biosensors have been developed to determine antimicrobial drug residues. Biosensors employs biological molecules, such as enzymes or antibodies, which is efficient for recognizing particular targeted analytes or residues. In the detection process, the molecules are paired to a transducer which responds to the reaction between the residue and the bound biological molecule. The resulting biochemical alert is observed optically or changed to electronic signal which is additionally clarified by suitable instrument. Biosensor tests are capable to identify concurrent multiclass antbiotics and pesticides in biological samples at a time. As Some authors described, that there is no need for sample cleanup for biosensor analytical technique (47).

High performance thin-layer chromatography (HPTLC)

HPTLC analytical technique allows the qualitative and quantitative determination of multi- drug residues in animal derived food products (meat and milk) but now days its applicability has rapidly decreased due to the development of other advanced techniques like HPLC (48). Reported uses of HPTLC applied to meat include the determination of veterinary drug residues like clenbuterol and other agonists (49), nitroimidazol and sulphonamides and thyreostatic drugs (50). During detection process the HPTLC plates are sprayed with proper chromogenic reagent or viewed under UV light for visualization of compounds. Detection by fluorescence is also applied. Quantitative analysis is achieved by measuring the relative intensity of the spot of sample *vs* that of the internal standard by scanning densitometry (50).

High Performance Liquid Chromatography (HPLC)

High performance liquid chromatography is a separation analytical technique. The principles of HPLC involves injection of a small volume of liquid samples into a tube (column) packed with tiny particles called the stationary phase. Individual components of the sample are moved down the packed column with a liquid (mobile phase) forced through the column by high pressure delivered by a pump. The sample components are separated from one another by the column packing that involves various chemical interactions between the molecules and the packing stationary phase. The separated components are detected at the exit of the column by a flow- through device (detector) that measures their amount. An output from this detector is called a liquid chromatogram (51).

High performance liquid chromatography is one of the most powerful analytical instrument in pharmaceutical analysis and analytical chemistry. HPLC has the ability to separate, identify and quantitate the compounds that are present in any sample that can be dissolved in a liquid. Compounds at very low concentrations (as low as parts per trillion) may be easily identified this technique. HPLC can be and has been, applied to just about any sample, such as pharmaceuticals, food, nutraceuticals, cosmetics, environmental matrices, and forensic samples (51).

HPLC usage is increasing day by day in the field of veterinary drug residue analysis in biological samples. HPLC have different mobile phases, vast library of column packings and the various modes of operations (52). HPLC was used for veterinary drug residue determination of oxytetracycline and penicillin G in milk in Ethiopia specifically samples collected from Nazareth dairy farms (53). From the of 400 milk samples, 48 milk samples were found to contain oxytetracycline and penicillin G in the range of 45–192 and 0–28 µg/l, respectively.

HPLC –DAD technique was also used for the determination of chloramphenicol, sulfonamide quinolones, and tetracyclines residues In Macedonia. a total of 497 raw milk samples were collected and the concentration of sulphonamides, quinolones and tetracycline in the range of 13.5-147.9, 0.6–22.0 and 17.4-149.1µg/kg, respectively (54).

A study was also conducted in Iran to determine the residues of tetracycle groups (tetracycline, oxytetracycline and chlortetracycline) from cattle tissue and organ, by using high performance liquid chromatography technique. The tetracycline concentration in Triceps muscle, gluteal muscle, diaphragm, kidney and liver were 176.3, 405.3, 96.8, 672.4 and 651.3 ng/g, respectively. The concentrations of tetracyclines were higher in liver and kidney sample compared to other sample (55) and it was higher in cured meat product (56).

Confirmatory methods for antibiotic residues

Confirmatory analytical methods or techniques for determination of veterinary drug residues or contaminants should provide actual information on the chemical structure of the residue or analytes. Analytical techniques based only on chromatographic analysis without the application of spectrometric detection are not appropriate on their own for use as confirmatory methods. However, if a single technique lacks sufficient specificity, the desired specificity may be achieved by analytical procedures

consisting of suitable combinations of clean-up, chromatographic separation(s, and spectrometric identification (48).

The LC-MS is the most commonly employed method for determination of veterinary drug residues in animal-derived foods products (57). The LC/MS technique uses LC as the separation system and MS as the detection system(58). It combines the high separation ability of chromatography for complex samples, and the advantages of MS with high selectivity, high sensitivity, and the ability to provide relative molecular mass and structural information to achieve rapid separation and determination of multiple residues (Table 2) (59).

Table 2
Antibiotic residues in different animal products

Name of the antibiotic	Matrix	Extraction technique	Purification technique	Detection system	Recovery (%)	Reference
Tetracycline	muscle	MSPD	Elution solvent: H_2O (70°C)	LC–MS/MS	99–103	(60)
Tetracycline	Milk	LLE	SPE (Oasis HLB)	LC–MS/MS	74–101	(61)
Tetracycline	Porcine kidney	MIPs	Elution solvent: MeOH:1M KOH (9:1, v/v)	HPLC-UV		(62)
Sulfonamide	Milk	LLE	Ultra-filtration	LC–MS/MS	90–125	(63)
Sulfonamide	Muscle	LLE	LLP (H2O:EtOAc)	UPLC–MS/MS	68–114	(64)
Quinolones	Bovine tissues	MSPD (sand)	Elution solvent: H2O (100 ◦C)	LC–MS/MS	87–109	(25)
Quinolones	Milk	MSPD (sand)	Elution solvent: H2O (100 ◦C)	LC–MS/MS	93–110	(58)
Quinolones	Eggs and tissue	MIPs	Elution solvent: ACN:TFA (99:1, v/v)	HPLC-FL	86–105	(65)
Aminoglycosides	Milk	MSPD (sand)	PLE	LC–MS/MS	70–92	(66)
Aminoglycosides	Muscle, liver	LSE	SPE (WCX)	LC–MS/MS	61–116	(67)
β-lactams	Bovine kidney	LSE	DSPE (C_{18})	LC–MS/MS	58–75	(57)
β-lactams	Milk	LLE	LLP	HPLC-UV	94–103	(68)
β-lactams	muscle	LSE	Ion-exchange SPE	LC–MS/MS	87–103	(69)

Conclusion

The repeated application of veterinary drugs for animals resulted to the occurrence of residues at various concentration levels in animal derived food products. In particular, antibiotic residues in dairy and meat industry may resulted in antibiotic resistance an extensive public health consequence. Deleterious effects of drug residues residing in animal derived food products may also induce carcinogenic and mutagenic effects and leads to the condition of antimicrobial allergy in the individuals who consume animal derived

food products. Accordingly, it is important to effectively control antibiotic residues in animal derived food products.

Declarations

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Competing interests

There is no conflict of interest

Ethical Approval

Not applicable

Consent for publication

Not applicable

Availability of data and material

As a literature review, we use published scientific papers across different journals

Authors' contributions

Feleke MG carried out the selection of literatures on antibiotic residues using different instrumental analysis, design of the study and participated in the write up. Abebe RB participated in the sequence alignment; write up and on the draft of manuscript preparation. Kasahun AE Participated in the selection, conceptualizing, coordination, write up and final draft of the manuscript.

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Figures

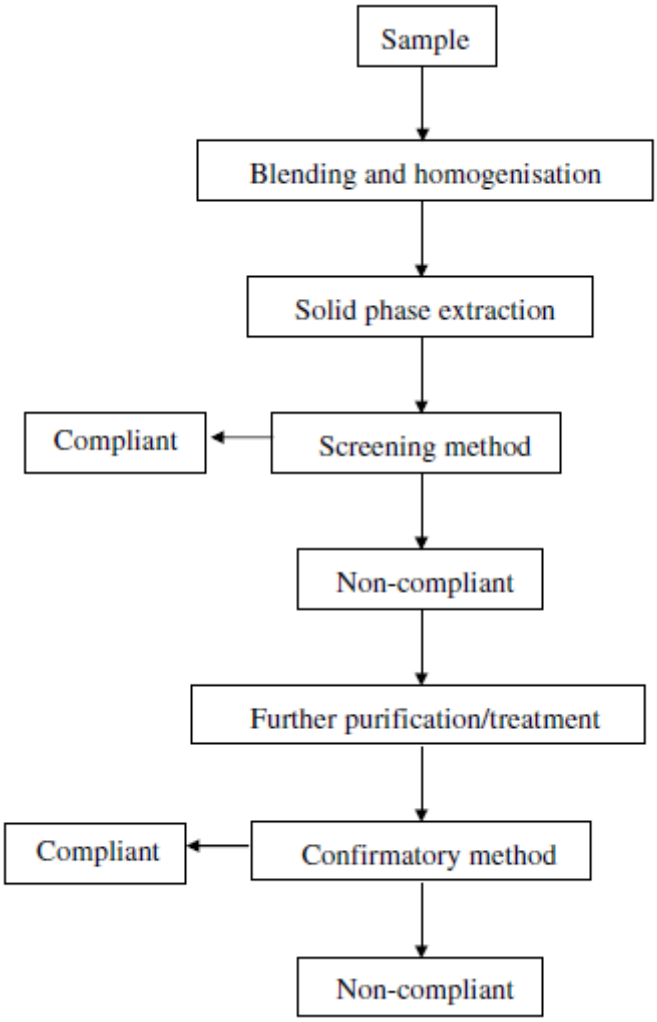

Figure 1

Example of typical processes for determination of a given analyte in a meat sample.