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Angelina Lopes Simões Pena

Resíduos de antibióticos em alimentos: Contribuição
analítica e avaliação da susceptibilidade bacteriana

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Doutora Maria Irene Noronha da Silveira

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INTRODUÇÃO GERAL

A utilização de medicamentos de uso veterinário e em particular dos que possuem acção antimicrobiana, tem vindo a aumentar significativamente nos últimos 30 anos.

Concretamente no que respeita à produção de animais produtores de alimento, as alterações ocorridas nas últimas décadas, conduziram a uma remodelação das estruturas produtivas onde dominam as explorações de média e grande dimensão e circuitos de comercialização, do produtor às indústrias transformadoras ou do produtor aos embaladores e armazenistas.

Assim, de forma a dar resposta efectiva às necessidades alimentares das populações, com o objectivo de manter elevado o nível de produção de alimentos de origem animal e de protecção das doenças infecciosas que os atingem, são cada vez mais utilizados antibióticos na moderna produção pecuária. Esta intensa utilização pode conduzir à presença de resíduos nos alimentos de origem animal por contaminação directa.

Os antibióticos são largamente administrados como agentes terapêuticos em medicina veterinária. São ainda utilizados como agentes profiláticos em animais, tanto em uso individual como ambiental, e como promotores de crescimento em animais destinados ao consumo humano.

Outras áreas potencialmente importantes de utilização incluem o tratamento ambiental em aquacultura e horticultura.

Neste contexto, a produção animal experimenta presentemente profundas alterações no conceito de qualidade e aceitação dos produtos de origem animal, por parte do consumidor cada vez mais atento e sensível aos aspectos da saúde pública.

A utilização de antibióticos em veterinária, é uma área de preocupação crescente e muito importante devido ao seu potencial impacto na saúde humana

O aspecto de grande importância e actualidade respeitante à utilização de antibióticos, surge agora como um nova e crescente preocupação que se tem vindo a desenvolver, face à revelação assustadora sobre a incidência das resistências antimicrobianas aos antibióticos.

A resistência bacteriana aos antibióticos é considerada como um problema sanitário de grande importância, a nível mundial. Esta foi uma das principais conclusões da Conferência de Copenhaga, em 1998, sobre a ameaça microbiana (Conferência de Copenhaga, 1998). Outras de carácter mais concreto e principalmente mais executivo, foram a necessidade de obter e processar dados procedentes da administração e consumo de antibióticos, assim como a adopção de um amplo leque de medidas destinadas a promover o uso prudente destes fármacos.

Deste modo, constitui preocupação fundamental, a obtenção de tecidos animais edíveis enquanto alimentos, isentos de resíduos de antibióticos que são nocivos para o consumidor.

É evidente a necessidade da utilização racional dos antibióticos, qualquer que seja a espécie animal alvo, de modo a promover a sua eficácia e evitar o desenvolvimento de resistências bacterianas, como consequência duma deficiente utilização dos antibióticos.

Todas as áreas de utilização dos antibióticos contribuem para a exposição dos microrganismos a estes medicamentos, embora a correlação entre a importância relativa de cada área de utilização, e o respectivo

consumo, e a emergência de resistências bacterianas aos antibióticos necessitem de um melhor esclarecimento.

Assim, a caracterização evolutiva dos padrões de dispensa de prescrição de antibióticos nas diversas áreas de utilização, enquanto dado científico concreto, é um elemento fundamental para a compreensão dos processos de desenvolvimento das resistências aos antibióticos.

Nas acções de combate à resistência bacteriana aos antibióticos, são indispensáveis sistemas globais e contínuos de vigilância. Relativamente à resistência aos antibióticos nos animais, deve ser feita referência, entre outras, às actividades do Comité de Medicamentos Veterinários da Agência Europeia de Avaliação dos Medicamentos (AEAM) que, habitualmente, examina a ocorrência de casos de resistência aos antibióticos em animais e a sua possível transferência ao homem. Além disso, deve ser feita uma menção ao programa de vigilância criado para dar cumprimento ao disposto no artigo 2º da Directiva 97/6/CE.

Recentemente, também foi criado um Sistema de Vigilância da Resistência aos Antimicrobianos (SVRA) e o Banco de Informação Global (BIG), desenvolvido no âmbito do programa de Controlo da Resistência aos Antimicrobianos da Organização Mundial de Saúde (OMS).

Os antibióticos são substâncias naturais, produzidas por microrganismos, que destroem ou impedem o desenvolvimento de outros microrganismos, enquanto que os agentes quimioterápicos são substâncias de síntese com as mesmas propriedades. O termo agente antimicrobiano foi definido como sendo qualquer substância de origem natural, semi-sintética ou sintética capaz de destruir um microrganismo. Para simplificar, nesta dissertação, e de acordo com o Parecer do Comité Económico e Social sobre “A resistência aos antibióticos: uma ameaça para a saúde pública”, os termos antibióticos e agentes antimicrobianos serão utilizados como sinónimos.

Entende-se por resíduo toda a substância activa, excipiente ou produto de decomposição e respectivos metabolitos, que permanecem no interior ou à superfície dos géneros alimentícios provenientes de animais, a

que tenham sido administrados medicamentos de uso veterinário (Regulamento do Conselho n.º 2377/90/CE).

O regulamento n.º 2377/90 de 26 de Junho, impõe o estabelecimento dos limites máximos de resíduo (LMRs), para todas as substâncias farmacologicamente activas, que fazem parte da composição dos medicamentos veterinários destinados a serem administrados a animais produtores de alimentos para consumo humano, de forma a proteger a saúde do consumidor.

Porém sobre esta matéria, não basta impor regras legislativas, é necessário promover um controlo laboratorial efectivo de pesquisa de resíduos através de uma metodologia devidamente validada para o efeito, de modo a determinar a natureza e a gravidade da contaminação com antibióticos e a avaliação do risco da sua ingestão.

Esta dissertação assenta em estudos desenvolvidos, agrupados em duas partes distintas e interligadas. Por um lado foi avaliada o impacto da utilização de antibióticos em suínos, tendo por objectivo dar um contributo para um melhor conhecimento da situação actual em Portugal. Encetou-se uma abordagem do problema da resistência das bactérias indicadoras aos antibióticos, isoladas dos animais em estudo, que decorre activamente, por uma utilização mais apropriada, mais responsável e mais prudente dos antibióticos em veterinária. Numa segunda parte, o desenvolvimento de metodologias analíticas conducentes à determinação, em particular, de resíduos de TCs de grande aplicação na prática veterinária, em diferentes matrizes alimentares.

Neste contexto, foi implementada uma metodologia analítica para a avaliação da segurança dos resíduos de antibióticos estabelecidos pelos LMRs máximos permitidos nos alimentos e métodos de avaliação da susceptibilidade bacteriana, em estirpes indicadoras isoladas nas fezes dos animais.

As tetraciclinas, são antibióticos de largo espectro, administrados nos animais produtores de alimento, no tratamento de doenças. Segundo os dados

de 1997 sobre o consumo de antibióticos em veterinária, fornecidos pela FEDESA, este grupo de antibióticos é extensamente utilizado na medicina veterinária.

A sua utilização pode resultar na presença de níveis elevados de resíduos de antibióticos nos produtos alimentares. Por este motivo, a monitorização de resíduos de tetraciclinas em alimentos de origem animal, deve constituir um programa de vigilância.

Os LMRs para as tetraciclinas estabelecidos pela Comunidade Europeia (CE) são de 600 µg/Kg no rim e 100 µg/Kg no tecido muscular e no leite. Os resíduos totais destas substâncias, tais como, a oxitetraciclina (OTC), a tetraciclina (TC), a clorotetraciclina (CTC) e a doxiciclina (DC), não devem ultrapassar estas concentrações. Recentemente, os LMRs estabelecidos para as tetraciclinas incluem a soma da tetraciclina e do seu epímero (Regulamento CE nº 508/1999).

A este respeito foi nossa intenção desenvolver nova metodologia de forma a proceder ao controlo laboratorial de pesquisa de resíduos de TCs. Neste âmbito foram realizados estudos conducentes ao desenvolvimento de métodos analíticos exactos, sensíveis, precisos e específicos, tendo sempre como objectivo a implementação de procedimento analítico simples.

O primeiro capítulo apresenta uma revisão sobre a prescrição e dispensa de medicamentos veterinários, a utilização de antibióticos em veterinária e os seus níveis de consumo, a sua regulamentação e as suas consequências na saúde do consumidor. Neste contexto a tónica foi colocada especialmente na emergência de resistências bacterianas aos antibióticos.

O segundo capítulo refere a revisão da metodologia analítica que envolve os processos de extracção, purificação, determinação e confirmação dos resíduos de tetraciclinas, nas diferentes matrizes alimentares, descritos na bibliografia científica.

Nos capítulos seguintes desenvolve-se a parte experimental desenvolvida nesta dissertação e os resultados obtidos:

- A avaliação da contaminação da carne de suínos por antibióticos e a sua possível correlação com a incidência de resistências aos antibióticos em bactérias indicadoras, isoladas nos animais em estudo, foi o tema abordado no capítulo III.

O capítulo IV versa o comportamento cromatográfico das TCs tendo sido estabelecida e validada a metodologia analítica por HPLC com detecção espectrofluorimétrica, para a determinação de resíduos de TCs em leites.

No capítulo V procedemos a estudos de avaliação dos processos de purificação por extracção em fase sólida e à validação de metodologias analíticas para a determinação de resíduos de TCs, em amostras de tecido muscular e rim de suínos, e de tecido muscular de salmão. Na análise de resíduos é essencial dispormos de metodologia analítica, que nos permita a identificação inequívoca dos compostos detectados. Deste modo desenvolvemos um método por HPLC-MS-APCI para a confirmação de resíduos de TCs.

Através de processos de degradação, as TCs podem produzir diversos metabolitos, alguns dos quais, são eles próprios, farmacologicamente inactivos, e mais tóxicos do que as suas moléculas precursoras, como é o caso da epianidrotetraciclina (EATC). Assim, cientes desta realidade, no capítulo VI procedemos em primeiro lugar, à validação de três métodos cromatográficos para a sua determinação, avaliando a sua adequação na análise deste tipo de compostos. Seleccionado o método cromatográfico, e aplicando a metodologia descrita em V, procedemos à sua determinação na amostra de tecido muscular de suíno. Numa segunda parte efectuou-se o desenvolvimento de um método que nos permitisse a detecção rápida dos produtos de degradação da TC (ETC, EATC e ATC), por

quimioluminescência.

O trabalho aqui encetado procurou contribuir para a análise da utilização dos antibióticos em veterinária, no sentido de dar voz a todo o trabalho que é necessário empreender no interesse da saúde de todos nós e dos animais, e do ambiente que nos acolhe.

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