DRUG ANALYTICAL RESEARCH
ISSN: 2527-2616 *www.seer.ufrgs.br/dar*

Quantitative analysis of pharmaceutical products by spectrophotometry in the infrared region: a practical review

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Quality control in the chemical-pharmaceutical industry to identify and quantify the active ingredient has fundamental importance to guarantee the quality of the final product. Its lack can generate irreparable consequences, and therefore its existence is extremely important. However, currently, in this process there is an ecologically correct need beyond the choice of the ideal method and the ideal conditions. This mini-review contemplates the current technological vision of pharmaceutical analysis through Green Analytical Chemistry (GAC). Green and sustainable methods have a main focus providing economic, environmental and social benefits. An example is spectrophotometry in the infrared region for quantitative purposes. The purpose of this mini-review is to show a practical guide for the quantitative analysis of raw materials and pharmaceutical products by spectrophotometry in the infrared region in order to contribute to a sustainability cycle, where the guarantee of product quality and the analytical awareness about health, time, waste generation, environment and cost coexist. A practical review for quantitative analysis by spectrophotometry in the infrared region was shown. It is useful for routine analysis of pharmaceutical products in general, and it can be used by chemical-pharmaceutical laboratories around the world.

Keywords: spectrophotometry in the infrared region; practical review; green analytical chemistry; quantitative analysis; pharmaceutical analysis; sustainable alternative.

Article received at 10/07/2022 and accepted at 11/07/2022.
https://doi.org/10.22456/2527-2616.127631

Introduction

Quality control is the sector responsible for monitoring the quality of the raw material on receipt, during storage, processing and final product. It is the sector responsible for approving batches of pharmaceutical products for the consumer market. Quality control is the first step to the correct use of medicines. It ensures the quality of a product using analytical techniques. Currently, the choice of method is not enough; the conditions involved in the analysis are also very important and should include the principles of Green Analytical Chemistry.

The Green Chemistry concept emerged in the 1990s and aimed to reduce pollution using so-called green solvents. In the late 1990s, the idea of Green Chemistry began to expand slowly in Europe and the United States, and its first concerns were chemical synthesis and chemical engineering (1). It evolved in each area and pharmaceutical analyses, which are included in analytical chemistry, gained 12 principles for collaborating with this fact (2-3).

Companies are investing heavily in the development and improvement of their processes, analyses and products, based on green analytical chemistry. The current sustainability scenario has been a growing worldwide concern, since national and international agencies, mediated by the United Nations, reached a consensus that Earth's resources are finite and pollution can have harmful effects on people and the planet. Another factor that encourages companies to invest in sustainable products and processes is the increase in costs for eliminating toxic wastes for pollution (3-4). For this reason, an ecologically correct, green and sustainable analytical method that reduces or eliminates the use of solvents or the generation of toxic waste for both the environment and the operator is essential (2-3, 5-9).

In this context, a prominent example is a method by spectrophotometry in the infrared region. It is a technique of excellence in the pharmaceutical sciences and is currently used for quantitative purposes (10-31). It is widely used by industries, research centers and areas of organic and inorganic chemistry as it is a simple, reliable technique and allows both to identify and quantify compounds (32-34).

Universities have played a fundamental role in serving as research centers, contributing to health control activities and scientific enrichment in the area. Thus, this mini-review shows an innovative practical guide for the quantitative analysis of raw materials and solid pharmaceutical products by spectrophotometry in the infrared region in order to contribute to a sustainability cycle, where product quality assurance and analytical awareness about health, time, waste generation, environment and cost coexist.

Practical review

The practical review was based on scientific articles (10-31), which used spectrophotometry in the infrared region for routine quantitative analysis of solid pharmaceutical materials (powder).

Among the examples, it is possible to mention the quantitative analysis to verify the content of darunavir (13), paracetamol (16), rifaximin (24), secnidazole (25) and enrofloxacin (27) in tablets; content of cefadroxil monohydrate (18) in capsules; content of ceftazidime (10), sodium ampicillin (11), sodium cefuroxime (12), sodium cefotaxime (20), daptomycin (21), sodium ceftriaxone (22), sodium ertapenem (26), sodium cephalothin (28), sodium cefazolin (29), cefepime hydrochloride (30) and vancomycin (31) in lyophilized powder; content of doxycycline (17) and norfloxacin (19) in raw material.

The technique by spectrophotometry in the infrared region presents different analysis methods. The method covered in this mini-review is the potassium bromide (KBr) pellet/tablet method. The use of KBr allows the control and homogeneity of the drug variable and consequently concentration. In addition to allowing the homogenization of samples, a fundamental step for a quantitative analysis.

The details for the applicability of the method in the context of quantitative pharmaceutical analyses are as follows:

a) As material: standard drug, sample and adjuvants. As diluent: potassium bromide (KBr).

b) An analytical balance to weight the powder, an agate mortar and pistil to homogenize the products, a compression system to prepare the tablets and an infrared spectrophotometer with suitable software will be needed.

c) First of all, the KBr must be crushed using agate mortar and pistil and then placed in the oven to dry for at least 24 hours. It will be used as a diluent in the preparation of tablets and each tablet will contain a total of 150 mg (drug + KBr).

A pool containing reference or sample or adjuvants should be prepared in ratio of 1:10 to minimize deviations. Then, tablets will obtain by weighting the different amount from this pool plus the diluent (KBr).

This mixture (pool + KBr) should be transferred to the compression system and let under compression for approximately 10 minutes at 90 kN; these conditions (time and compressive strength) must be optimized for each case. After this period, tablets should be set in the spectrophotometer compartment for absorbance readings.

The processes described above are illustrated in Figure 1.

d) In a first step, the spectra will be analyzed in transmittance to evaluate the product profile, characteristic bands and compatibility of the bands present as described in the literature. This study must be carried out for each individual product and later it must be done by comparing equivalent and particular bands. The objective is to find a band or point that is specific to the standard + present in the sample + absent in the adjuvants.

In this stage of defining the band or point that will serve to quantify the drug content, it is interesting to subject the sample to stressful conditions and to compare its spectrum with the spectrum of a full sample (no degradation). This must be taken into consideration when choosing the band or point and will make the method indicative of stability. The stressful condition will depend on the characteristics of each drug or product and can be UV light or heat.

In a second step, the spectra will be analyzed through the absorbance values provided in the range or band point chosen. With these absorbance values it is possible to quantify the sample using a standard.

The steps described above are illustrated in Figure 2.

Discussion

Following the steps recommended in the previous item, it is possible to quantify drugs and pharmaceutical products in an advantageous, reliable and effective way. However, the choice of method conditions must be carefully made.

The technique involves characteristics of green analytical chemistry, which makes it current and sustainable. It has the advantages:

a) a single low cost reagent (KBr) is required in small quantities, which makes the process economical and fast

b) KBr presents low health risk, does not burn, is stable and is a non-flammable reagent, according to the Hommel Diagram

c) no need for disposable materials, which makes the process economical and sustainable

d) no need for equipment conditioning time, which makes the process fast

e) the equipment does not require frequent maintenance, which makes the process economical

f) training to handle it is simple and easy, which expands the use for several collaborators

g) results are obtained in seconds, which makes the process fast and economical, since more samples can be analyzed

h) the speed of the process also contributes to the use of less energy and makes the employee's time available for other activities

i) automated system

j) indicative of stability

k) possibility of working with small concentrations around µg

l) possibility to analyze poorly soluble and insoluble samples

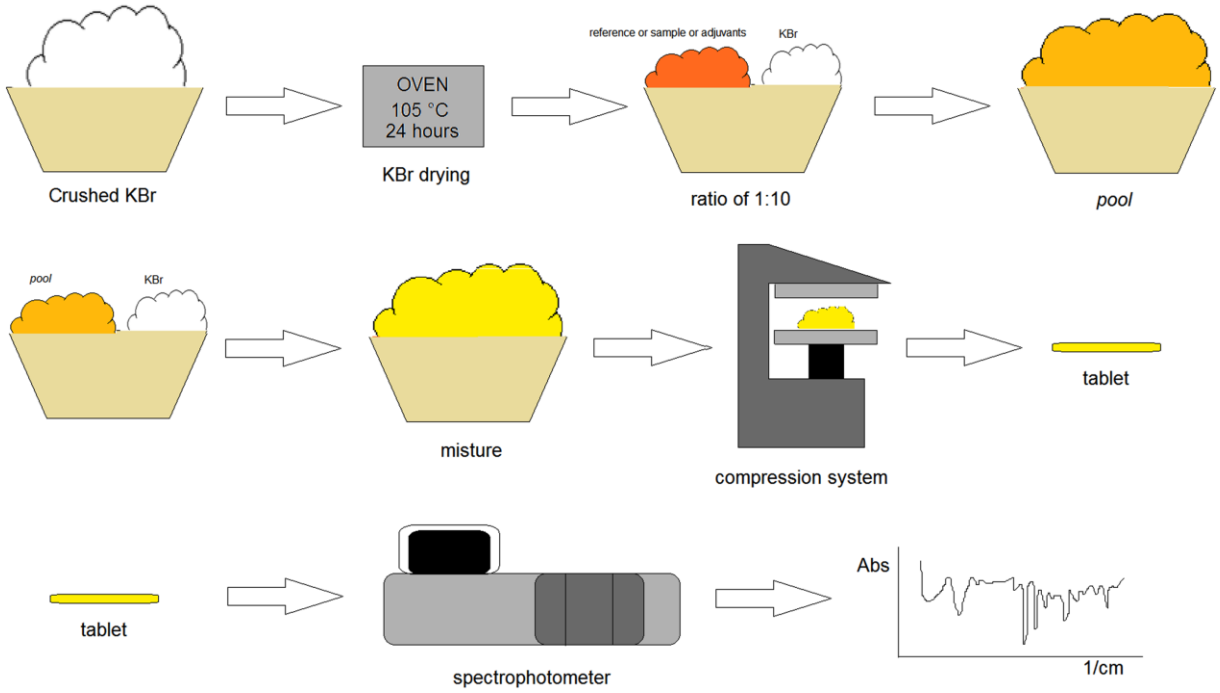

Figure 1. Process of preparing the tablets for quantitative analysis by spectrophotometry in the infrared region.

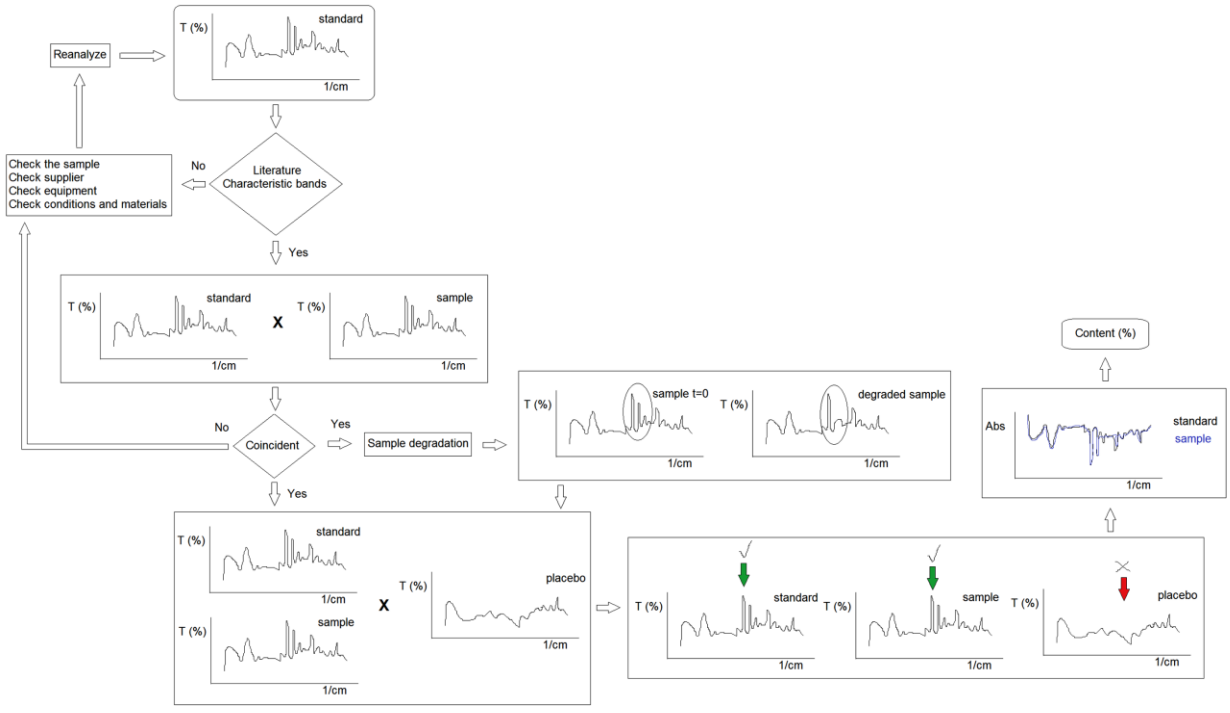

Figure 2. Flowchart of the analysis of the infrared spectrum for quantitative purposes.

Spectrophotometry in the infrared region for qualitative purposes is consecrated in pharmaceutical analysis. On the other hand, for quantitative purposes it is still not a priority in the chemical-pharmaceutical industries. Its high specificity can be an important tool for quantitative analysis as well. Liquid chromatography is the technique of choice today and the idea of this mini-review is not to change that. After all, each technique has its own characteristics and the choice to use one or the other must be based on the intended analysis and what you want to verify or study.

The intention of this mini-review is to present a fast, economical, reliable and eco-friendly way to perform routine quantitative analysis of drugs and pharmaceutical products by mid-infrared. It gathers the best actions and the most effective choices from other works in the literature (10-31) for the quantitative analysis of a pharmaceutical product using spectrophotometry in the infrared region, also considering the indication of stability of this product, as it takes into account the sample degradation analysis (Figure 2).

The option of having a quantitative method by mid-infrared that is ecologically correct, low-cost, fast, reliable, effective and indicative of stability in the laboratory routine of pharmaceutical product analysis is extremely advantageous for the company as a whole. For example:

a) Treating less waste and/or less toxic waste is cheaper.

b) Using less reagents and/or no need for disposable materials makes the method cheaper as well.

c) Faster methods impact the release of results faster, which streamlines the entry of products on the market.

d) Infrared equipment is robust and easy to handle, which affects the cost of analysis.

e) Methods indicative of stability can be developed and validated, as stated in this practical review, which enhances the analysis.

To sum up, all these consequences are the advantages of the proposed guide.

Conclusions

This practical review is useful to guide quantitative analysis of drugs and solid pharmaceutical products by spectrophotometry in the mid-infrared region. It also positions the technique in the current context of green and sustainable analytical chemistry. This mini-review can be used by laboratories and chemical-pharmaceutical industries around the world.

Conflict of interest

The authors declare no conflicts of interest.

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