

Errors in pharmaceutical analysis



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The logo of Galgotias University is a circular emblem with a stylized 'G' shape in the center. The 'G' is composed of three curved segments in shades of yellow, blue, and red. The background of the emblem is a gradient of light blue and white.

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Introduction

Classification of errors

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a. Determinate Errors

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b. Indeterminate Errors

Accuracy

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Precision

◆

Minimizing Systematic Errors

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Error

Error is the difference between the true result (or accepted true result) and the measured result.

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If the error in an analysis is large, serious consequences may result. As reliability, reproducibility and accuracy are the basis of analytical chemistry.

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A patient may undergo expensive & even dangerous medical treatment based on an incorrect laboratory result because of an analytical error.

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Error= measured mean value – true value

true value

- ◆ And the difference between the experimental value and true value is termed as **absolute error**.
- ◆ Absolute error may be negative or positive.

Types of errors :

There are two principle types of error in analysis :

- ◆ Determinate or systematic error
- ◆ Indeterminate or random error

DETERMINATE ERROR

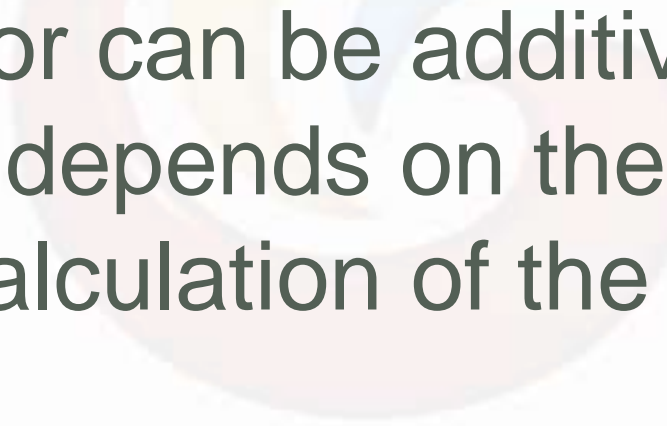
- ◆ They are caused by faults in the analytical procedure or the instruments used in the analysis.
- ◆ Determinate errors are systemic errors i.e. they are not random.
- ◆ As the name indicates that the cause of this type of error may be found out & then either avoided or corrected.

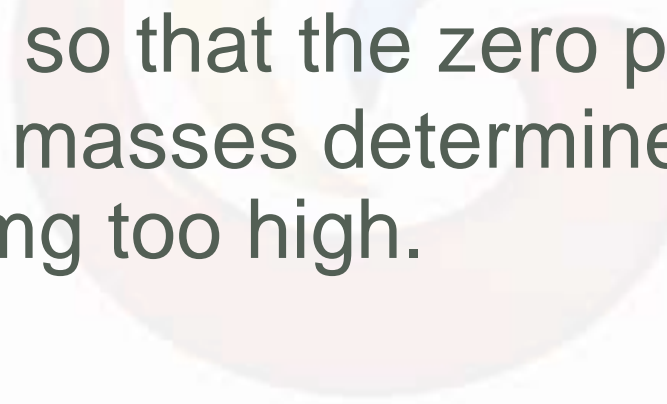
A particular determinate error may cause the analytical results produced by the method to be always too high.

Another determinate error may render all results too low.

Sometimes the error remains constant;

All results are too high or too low by the same amount.

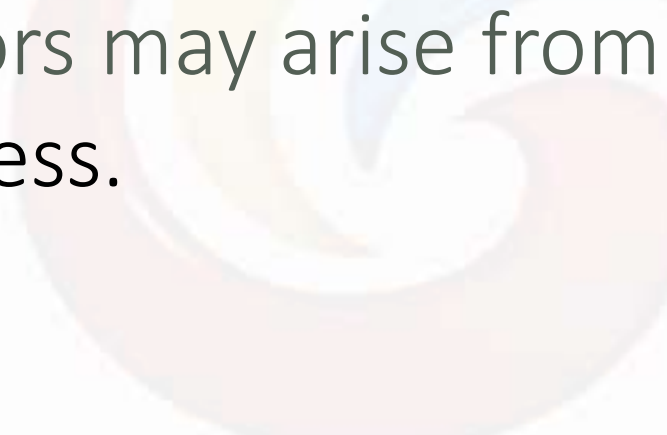
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- The logo of Galgotias University is a circular emblem with a stylized 'G' in the center. The 'G' is composed of several curved, overlapping bands in shades of orange, yellow, and blue. The background of the emblem is a light, textured pattern.
- ◆ Determinate error can be additive or they can be multiplicative . It depends on the error & how it enters into the calculation of the final result.
 - ◆ This determinate error could be the result of an incorrectly calibrated balance.

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- ◆ If the balance is set so that the zero point is actually 0.5 mg too high, all masses determined with this balance will be 0.5mg too high.
 - ◆ If this balance was used to weigh any std. sol. Used in the laboratory, the std. concentration will be erroneously high, and all of the results obtained using this std. will be erroneously high.

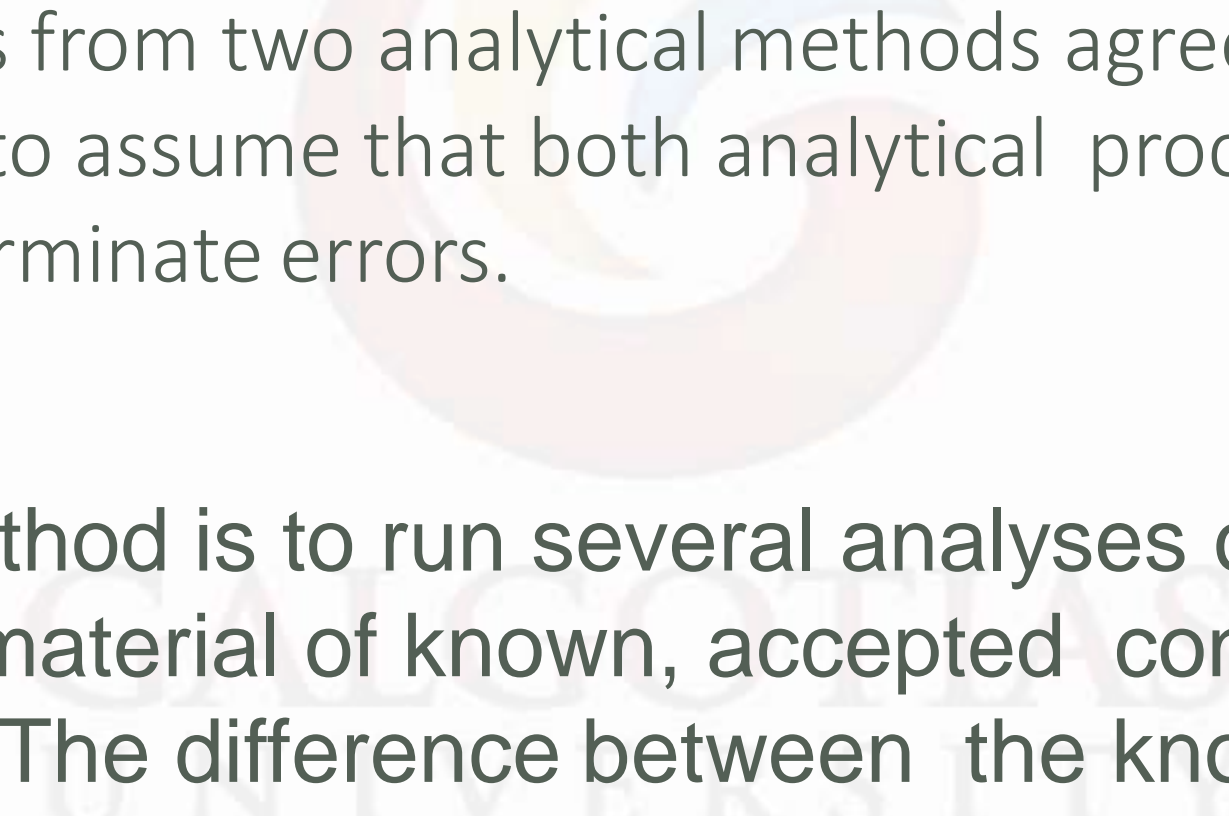
- ◆ The error is reported as the absolute error, the absolute value $|x - y|$ is the difference between the true and measured value.

Measured mean value – True value =

Absolute error

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- ◆ Determinate errors may arise from some faulty step in the analytical process.
 - ◆ The faulty step is repeated every time the determination is performed. Whether a sample is analyzed 5 times or 50 times, the results may agree with each other but differ widely from the true answer.

- ◆ Systemic error is under the control of the analyst.
- ◆ **How are determinate errors identified and corrected...?**
- ◆ One is to analyze the sample by a completely different analytical procedure that is known to involve no systematic errors. Such methods are often called “standard methods”; they have been evaluated extensively by many laboratories & shown to be precise and accurate.

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- ◆ If the results from two analytical methods agree, it is reasonable to assume that both analytical procedures are free of determinate errors.
 - ◆ The 2nd method is to run several analyses of a reference material of known, accepted concentration of analyte. The difference between the known concentration and that measured by analysis should reveal the error.

If the results of analysis of a known reference std. are consistently high or low, then a determinate error is involved in

- ◆ the method.

Determinate error can arise from uncalibrated balances, improperly calibrated volumetric flasks or pipettes, malfunctioning instruments, impure chemicals, incorrect analytical procedures or techniques and analyst error.

Analyst error : They may be the result of inexperience, insufficient training.

- ◆ An analyst may use the instrument incorrectly,
- ◆ Perhaps by placing the sample in the instrument incorrectly each time.
- ◆ Setting the instrument to the wrong conditions for analysis.
- ◆ Misreading a meniscus in a volumetric flask as high(or low)

Operational and Personal errors :

- ◆ These are due to factors for which the individual analyst is responsible and are not connected with the method or procedure they form part of the **personal equation** of an observer.

Examples are:

- ◆ Mechanical loss of materials in various steps of analysis.
- ◆ Underwashing or over washing of precipitates.
- ◆ Ignition of ppts at incorrect temperatures.

Some analyst are unable to judge color changes sharply in visual titrations, which may result in slight overstepping of the end point.

Some other analyst – related errors are :

Carelessness

Transcription errors, i.e. copying the wrong information into a lab notebook or onto a label.

Proper training, experience, and attention to detail on the part of the analyst can correct these types of errors.

Reagents and instrumentation :

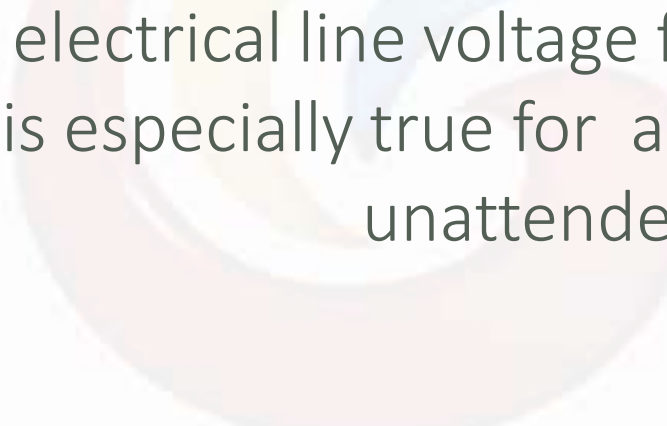
- ◆ Contaminated or decomposed reagents can cause determinate errors.
- ◆ Prepared reagents may also be improperly labeled.

Impurities in the reagents may interfere with the determination of the analyte, especially at the ppm level or below.

- ◆ Numerous errors involving **instrumentation** are possible, including
 - ◆ Faulty construction of balances,
 - ◆ Incorrect instrument alignment,
 - ◆ Incorrect wavelength settings,
 - ◆ Use of uncalibrated or improperly calibrated weights.

These problems can be eliminated by a systematic procedure to check the instrument settings and operation before use. Such procedures are called **std. operating** (SOPs) in the many labs.

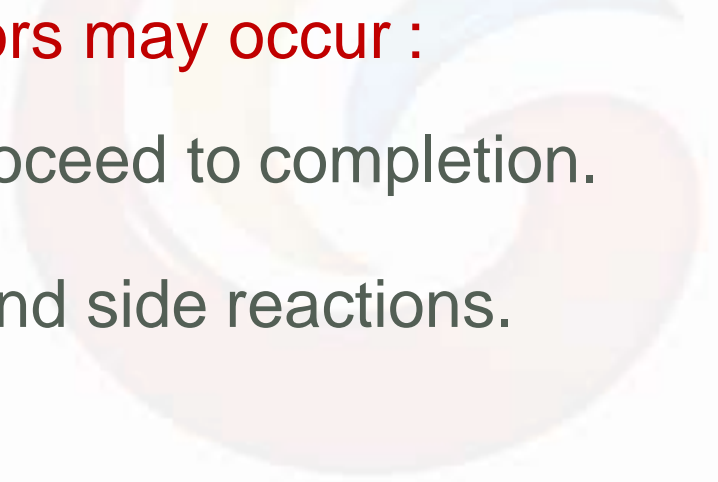
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- ◆ In instrumental analysis, electrical line voltage fluctuations are a particular problem. This is especially true for automated instruments running unattended overnight.
 - ◆ Instruments are often calibrated during the day, when electrical power is in high demand.
 - ◆ At night , when power demand is lower, completely changing the relationship between conc. Of analyte and measured signal.

- ◆ **Analytical Method** :The most serious errors are those in the method itself.

Examples of method include

- ◆ Incorrect sampling
- ◆ Incomplete reaction for chemical methods,
- ◆ Unexpected interferences from the sample itself or reagents used.
- ◆ Loss of analyte during sample preparation by volatilization or precipitation.

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- **In titrimetric analysis errors may occur :**
 - Failure of reactions to proceed to completion.
 - Occurrence of induced and side reactions.

 - **In gravimetric analysis:**
 - Decomposition
 - co- precipitation and post – precipitation.
 - Precipitation of constituents other than the desired ones.



◆ **Contamination:**

Contamination of sample by external sources can be a serious source of error and may be extremely variable.

Aluminum levels in the dust in the normal laboratory are so high that dust prohibits the determination of low ppb levels of aluminum in samples.

Indeterminate

errors :

- ◆ Indeterminate errors can not be pin- pointed to any specific well defined reasons.
- ◆ They are random in nature & take place in several successive measurements performed by the same analyst under the same conditions and identical experimental parameters.

Sources of random error include the limitations of reading balances, electrical noise in instruments and vibrations caused to the building by heavy vehicular- trafficking , which are beyond anyone's control.

For eg. A balance that is capable of measuring only to 0.001 g can not distinguish between two samples with masses of 1.0151 & 1.0149 g.

In one case the measured mass is low, in the other case it is high.

ACCURACY :

- ◆ An accurate result is the one which matches very nearly with true value of a measured amount.
- ◆ Accuracy is inversely proportional to the error i.e. the greater the accuracy, smaller is the error.

PRECISION:

- ◆ Agreement among a cluster of experimental results however it does not imply anything with respect to their relation to the true value.
- ◆ Precision designates **reproducibility** of a measurement, whereas accuracy the **correctness** of a measurement.

Minimizing systematic errors:

- ◆ Calibration of instruments, apparatus and applying necessary corrections:
- ◆ Instruments commonly used in lab, such as spectrophotometer, electrical balance etc must be calibrated before use.
- ◆ Pipettes, burettes, volumetric flasks, thermometers must be calibrated.

Reference

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