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Research Article

ELEMENTAL ANALYSIS OF ANALGESIC DRUGS USING WAVELENGTH- DISPERSIVE X-RAY FLUORESCENCE SPECTROMETRY

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ABSTRACT

Analgesics are used in the treatment of a wide variety of medical conditions. This paper discusses the elemental composition and concentration of analgesic drugs by wavelength dispersive X-ray fluorescence. Physical basis of used analytical method, experimental set up and the procedure of sample preparation are presented. The complete results of this investigation are given in Table 1. The presence of C, O, Mg, Si, Cl, Ti, Fe, Na, S, Ni, P, K, Pd, Ca, Mn, Al, Crelements in analgesic drugs were found. The relative errors for results have been given 7 %. Wavelength-dispersive X-ray fluorescence spectrometry is a proven technique to determine the presence of various elements in analgesic drugs.

Keywords: Wavelength-dispersive X-ray fluorescence, Analgesic Drugs, Elemental concentration,

INTRODUCTION

Analgesics are used in the treatment of various pain syndromes and other medical conditions. Analgesics may be classified into two types: anti-inflammatory drugs and the opioids. Most anti-inflammatory analgesics are derived from three compounds discovered in the 19th century—salicylic acid, pyrazolone and phenacetin (or acetophenetidin). Although chemically unrelated, the drugs in these families have the ability to relieve mild to moderate pain through actions that reduce inflammation at its source. Acetylsalicylic acid, or aspirin, which is derived from salicylic acid, is the most widely used mild analgesic. It is considered the prototype for anti-inflammatory analgesics, the two other major types of which include acetaminophen (a derivative of phenacetin) and the aspirin-like drugs, or nonsteroidal anti-inflammatory drugs(NSAIDs) which include compounds such as ibuprofen, naproxen, and fenoprofen. Pyrazolone derivatives, with some exceptions, are no longer widely used in many countries, because of their tendency to cause an acute infection known as agranulocytosis.

The opioid analgesics were once called narcotic drugs because they can induce sleep. The opioid analgesics can be used for either short-term or long-term relief of severe pain. In contrast, the anti-inflammatory compounds are used for short-term pain relief and for modest pain, such as that of headache, muscle, strain, bruising, or arthritis.

The term *opioid* has been adopted as a general classification of all those agents that share chemical structures, sites, and mechanisms of action with the endogenous opioid agonists (endogenous substances are those produced inside the human body). Opioid substances encompass all the natural and synthetic chemical compounds closely related to morphine, whether they act as agonists (cellular activators) or antagonists (substances that block the actions of agonists). Although interest in these drugs had always been high because of their value in pain relief and because of problems of abuse and addiction, interest intensified in the 1970s and ’80s by discoveries about the naturally occurring morphinelike substances, the endogenous opioid neuropeptides.

Analgesics are the most commonly consumed over-the-counter drugs in the world. The need for drug concentration determination becomes critical in situations where overdose, abuse, or toxicity is suspected. Various analgesics have been studied for determination active ingredients such as caffeine, salicylamide, acetaminophen, aspirin etc. Several methods such as High Performance Liquid Chromatograpy (HPLC) (Beaver et al., 1983; Süzen et al., 1999), near infrared transmittance (Eustaquio, 1999), Transmission FT-IR spectroscopy (Khaskheli, 2013), Raman spectroscopy (Mazurek and Szostak, 2011), FT-NMR (Schmedake and Lawrence, 1996), mobility spectrometry (Verkouteren and Staymates, 2011), derivative spectrophotometric methods (Paschoal and Ferreira, 2000; Erk et al., 2001) have been reported for the determination active ingredients. But analgesic drugs can be examined for inactive, inorganic ingredients which are frequently found in greater than trace amounts (>1%).The analysis of analgesic drugs using wavelength-dispersive X-ray fluorescence spectrometry is as yet not made. Therefore, this study focuses on the analysis of analgesic drug using wavelength-dispersive X-ray fluorescence spectrometry.

The most important advantages of the use of wavelength dispersive x-ray fluorescence for the quantitative and qualitative analysis are

-simultaneous determine of many elements,

It has an extremely good sensitivity for all elements from B to U in qualitative analysis and determined the wide concentration range in quantitative analysis.

-the possibility to determine in a wide concentration range,

-the sample preparation is simple and fast

2. Experimental Procedure

The analysis of elements present in analgesics was carried out by WDXRF. A schematic of the WDXRF system is given in Fig. 1.

A Rigaku wavelength- dispersive X- ray fluorescence spectrometer (ZSX-100e) with the established instrumental conditions, such as voltage (kV), current (mA), collimators, filters, attenuator, analyze crystal, detector, 12 positions and fixed counting time for Rh anode tube was used.

Analgesics were taken from pharmacy. Analgesics were ground and sieved to a mesh size of 100 μm. A 10 ton hydraulic press was used to compress the sample powders into thin pellets of 12 mm diameter. Mass thickness of soil samples was chosen as 0.2 - 0.3 g/cm^2 to reduce the matrix effect. The advantage of making these pellets is that inter-element enhancement effects in the sample are minimised. The effects of the matrix composition on the measured analyte-line intensity are known as matrix-, inter-element-, self-absorption- and absorption-enhancement effects. Whatever absorption-enhancement effects a specified analyte-matrix system may be subject to, they increase with increasing thickness, decrease with decreasing thickness, and essentially disappear in thin samples (Bertin, 1970). Each sample is then radiated for about 1 hours.

3. RESULTS AND DISCUSSION

Qualitative analysis chart acquired by A Rigaku wavelength- dispersive X- ray fluorescence spectrometer (ZSX-100e) for aspirin is presented in Fig2 as an example. The mean concentrations with relative error (7%) obtained for analgesics using WDXRF are shown in Table 1.

The findings obtained in this study are important for human health. By WDXRF technique, it was measured the elements C, O, Mg, Si, Cl, Ti, Fe, Na, S, Ni, P, K, Pd, Ca, Mn, Al, Cr in analgesic drugs.

These elements are essential to humans. Both deficiencies and excesses of these elements may result in a number of disorders in the human body. On the other hand the toxic elements are known to be very harmful even at extremely low concentration. For this reason, reliable analyses will help to clarify and define effective treatment.

It can be noted that magnesium was higher in Dispril. The magnesium concentration of in Dispril is$1.069\pm7.48x10^{-2}$ %.

Chloride were found large amounts in both Voltaren and Dicloflam. The chloride concentrations of in Voltaren and Dicloflamare 53.040± 3.713 % and 16.544 ± 1.158 %, respectively. Some studies claim that high chlorine levels increase the risk of bladder cancer and incidence of Hodgkin's disease, colorectal, oesophageal and breast cancer. According to these studies, women with breast cancer have 50% to 60% higher levels of organochlorines (chlorination by products) in their breast tissue compared to women without breast cancer. Chlorine has also been associated with declining sperm counts and male infertility.

As seen in Table 1, high Na concentration was observed in Aspirin Plus C.The sodium concentration of in Aspirin PlusC is 15.88 ± 1.112 %.

As seen from results of analysis, phosphorus concentration was observed in Nurofen. The phosphorus concentration of in Nurofen is

9.654 ± 0.676 %. Phosphorus is essential for life. As phosphate, it is a component of DNA, RNA, ATP, and also the phospholipids that form all cell membranes. Demonstrating the link between phosphorus and life, elemental phosphorus was historically first isolated from human urine, and bone ash was an important early phosphate source.

Sulphur concentration in Melort was found as 6.401 ± 0.448 %. Sulfur is an essential element for all life, and is widely used in biochemical processes. In metabolic reactions, sulfur compounds serve as both fuels (electron donors) and respiratory (oxygen-alternative) materials (electron acceptors). Sulfur in organic form is present in the vitamins biotin and thiamine. Sulfur is an important part of many enzymes and in antioxidant molecules likeglutathione and thioredoxin. Organically bonded sulfur is a component of all proteins, as the amino acids cysteine and methionine. Disulfide bonds are largely responsible for the mechanical strength and insolubility of the protein keratin, found in outer skin, hair, and feathers.

Silicon concentration in Dicloflam was found as 3.589 ± 0.251 %.

Iron concentration in Kalidren was found as 0.476 ± 0.033 %. Iron plays an important role in biology, forming complexes with molecular oxygen in haemoglobin and myoglobin. These two compounds are common oxygen transportproteins in vertebrates.

Titanium concentration in Voltaren was found as 0.520 ± 0.0364 %.

Calcium concentration in Dispril was found as 0.520 ± 0.0364 %. Calcium is now the most promoted nutrient by proponents of conventional, nutritional and alternative medicine- yet at the same time, the assumed need is based purely on the speculation that the body's calcium intake is well below its requirements. Of the approximately 1 g of calcium in the average 70 kg adult body, almost 98% is found in bone, 1% in teeth and the rest is found in blood, extra cellular fluids and within cells where it is a co-factor for a number of enzymes. Calcium promotes blood clotting by activating the protein fibrin and along with magnesium helps to regulate heartbeat, muscle tone, muscle contraction and nerve conduction. Chronic calcium deficiency is associated with some forms of hypertension, prostate and colorectal cancer, some types of kidney stones, and miscarriage, Birth (heart) defects are seen in children when mother has periodontal disease, sleep disturbances, mental health / depressive disorders, cardiovascular or hemorrhagic diseases. Elevated calcium levels are associated with arthritic and vascular degeneration, calcification of soft tissue, hypertension and stroke, gastrointestinal disturbances, mood and depressive disorders, chronic fatigue, increased alkalinity and general mineral imbalances. High calcium levels interfere with vitamin D and subsequently inhibit the vitamin's cancer-protective effect unless extra amounts of vitamin D are supplemented.

There are some problems with analgesic use. Nearly all analgesic drugs exhibit some type of undesirable side effect. There are many types of potential side effects, such as addiction, drowsiness, allergic reactions, and dry mouth. In some cases, side effects can be fatal. In many cases, analgesic drugs are approved when side effects occur in only a very small percentage of the population, or are relatively mild. However, somewhat severe side effects can be tolerated if the analgesic drug is extending life expectancy for patients with an otherwise fatal condition.

Appropriate dosage varies by analgesicdrug and should consider the type of pain, as well as other risks associated with patient age and condition. For example, narcotic analgesics should usually be avoided in patients with a history of substance abuse but may be fully appropriate in patients with cancer pain. Similarly, because narcotics are more rapidly metabolized in patients who have used these drugs for a long period, higher than normal doses may be needed to provide adequate pain management.

Also, parents of children taking analgesics should review adverse effects of each drug individually. Drugs within a class may vary in their frequency and severity of adverse effects. The primary adverse effects of the narcotic analgesics are addiction, constipation, and poor respiratory function. Because narcotic analgesics stimulate the production of enzymes that cause the metabolism of these drugs, patients on narcotics for a prolonged period may require increasing doses. This physical tolerance is not the same thing as addiction and is not a reason for withholding medication from patients in severe pain.

NSAIDs may cause kidney problems. Gastrointestinal discomfort is common, although in some cases, these drugs may cause ulcers without the prior warning of gastrointestinal distress. NSAIDs may cause blood to clot less readily, although not to the same extent as if seen with aspirin.

Most users of acetaminophen experience few, if any, side effects. But the drug can cause liver damage, especially when taking

too much or if taken with alcohol. Because acetaminophen is present in many medications, from cold medicines and over-the-counter pain relievers to prescription drugs such as Percocet and Vicodin, users may not realize they are taking too much.

Opioid analgesics cause numerous side effects, including drowsiness, dizziness, respiratory depression, constipation, and urinary retention. Some of these effects will disappear with continued use or may be managed with other medications (constipation). Others, including urinary retention, may not. In addition, opioid use may lead to addiction or dependence, and patients often develop a tolerance to the drugs' analgesic effects. Upon withdrawal, dependent patients may experience a host of unpleasant side effects, including shivering and diarrhoea.

4. CONCLUSIONS

In this study, quantitative and qualitative analysis of analgesic drugs were taken from pharmacy. Through analysis using wavelength dispersive X-ray fluorescence spectrometer, the elements of: C, O, Mg, Si, Cl, Ti, Fe, Na, S, Ni, P, K, Pd, Ca, Mn, Al, Cr were detected in the analgesic samples.

The wavelength dispersive X-ray fluorescence spectrometer (WDXRF) provides superior analytical performance for most demanding tasks regarding accuracy, precision, speed and reliability in industrial and scientific research.

The wavelength dispersive X-ray fluorescence spectrometer (WDXRF) fluorescence spectrometer is unrivaled in elemental analysis of inanimate substances. Detection and the maximum achievable precision and accuracy limits bring limitations on the applications of XRF (Van Grieken, 1993). The recent advent of commercially available wavelength-dispersive spectrometers for X-ray fluorescence (XRF) measurements has provided an economical and powerful tool for environmental, clinical, chemical, geological and industrial analysis. XRF is a non-destructive, fast, multi-element technique for analyzing the surface layer and determining major, as well as minor elements, in thin and thick samples of all sizes and forms.

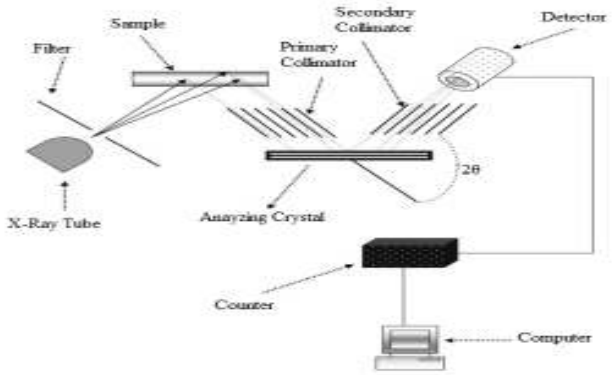

Fig. 1: The experimental setup

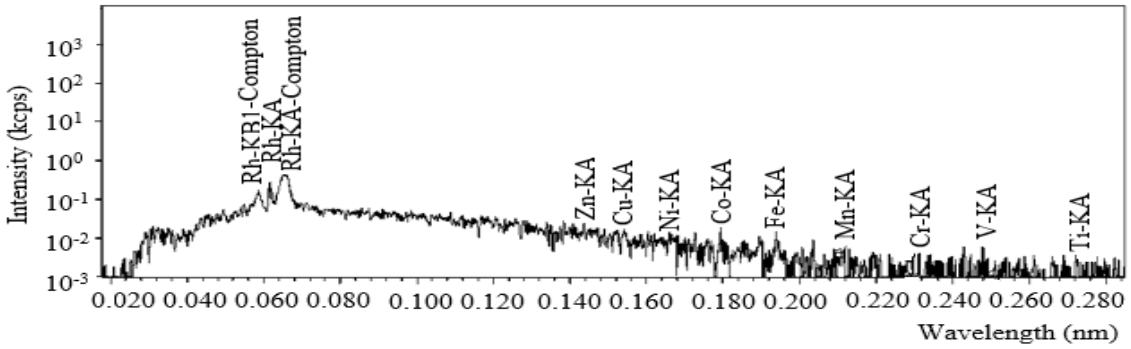

Fig. 2: Qualitative analysis chart acquired by A Rigaku wavelength- dispersive X- ray fluorescence spectrometer (ZSX-100e) for aspirin

Table 1: The mean concentrations with relative error (7%) obtained for analgesics

	C	O	Mg	Si	Cl	Ti	Fe	Na	S	Ni	P	K	Pd	Ca	Mn	Al	Cr
Aferin	53.493 ±3.744	44.445 ±3.111	0.390 ±0.027	0.812 ±0.056	0.591 ±0.041	0.227 ±0.016	0.025 ±0.001	-	-	-	-	-	0.013 ±0.001	-	-	-	-
Arvalese	34.507 ±2.415	63.349 ±4.434	-	-	1.111 ±0.077	0.125 ±0.008	0.054 ±0.004	0.817 ±0.057	0.019 ±0.001	0.015 ±0.001	-	-	-	-	-	-	-
Asp. Plus C	19.434 ±1.360	64.626 ±4.523	-	-	0.100 ±0.007	-	-	15.88 ±1.111	-	-	-	-	-	-	-	-	-
Aspirin	40.306 ±2.821	59.679 ±4.177	-	-	-	-	-	-	-	-	0.013 ±0.001	-	-	-	-	-	-
Dicloflam	5.951 ±0.416	34.848 ±2.439	1.055 ±0.073	3.589 ±0.251	16.544 ±1.158	-	-	0.326 ±0.022	0.022 ±0.001	-	8.739 ±0.611	-	-	-	-	-	-
Dispril	14.568 ±0.010	55.001 ±3.850	1.069 ±0.074	1.195 ±0.083	-	-	-	-	0.600 ±0.042	-	-	-	-	27.522 ±1.926	-	0.044 ±0.003	-
Etol	49.580 ±3.470	49.176 ±3.442	0.437 ±0.030	0.558 ±0.039	-	0.213 ±0.014	0.022 ±0.001	-	-	0.010 ±0.001	-	-	-	-	-		-
Kalidren	53.695 ±3.758	45.707 ±3.199	-	-	-	-	0.476 ±0.033	-	-	0.051 ±0.004	-	-	0.012	-	-		0.056
Majezik 100	33.549 ±2.348	63.636 ±4.454	0.138 ±0.010	2.077 ±0.145	-	0.439 ±0.030	0.111 ±0.008	-	-	0.013 ±0.001	-	0.033 ±0.002	-	-	-		-
Mazejik 200	67.889 ±4.752	31.526 ±2.206	-	-	0.206 ±0.014	-	0.313 ±0.021	-	0.020 ±0.001	0.042 ±0.003	-	-	-	-	-		-
Maxaljim	34.007 ±2.380	63.631 ±4.454	0.217 ±0.015	1.289 ±0.090	-	-	-	-	0.031 ±0.002	-	0.022 ±0.001	-	-	0.035 ±0.002	-	-	-
Melort	34.097 ±2.386	55.561 ±3.889	0.244 ±0.017	2.618 ±0.183	-	-	-	1.055 ±0.073	6.401 ±0.448	-	0.021 ±0.001	-	-	-	-	-	-
Musco-flex	32.807 ±2.296	66.341 ±4.643	0.279 ±0.019	0.034 ±0.002	0.090 ±0.006	-	0.019 ±0.001	-	0.394 ±0.027	-	-	0.023 ±0.002	-	-	-	-	-
Nsaid-Flurbi	33.869 ±2.370	63.813 ±4.466	-	2.099 ±0.146	-	0.216 ±0.015	-	-	-	-	-	-	-	-	-	-	-
Nurofen	14.866 ±1.040	30.727 ±2.150	0.361 ±0.025	0.047 ±0.003	-	-	-	0.992 ±0.069	-	-	9.654 ±0.675	-	-	-	-	0.031 ±0.002	-
Parol	50.450 ±3.531	49.015 ±3.431	-	0.215 ±0.015	0.091 ±0.006	-	0.154 ±0.011	-	0.046 ±0.003	0.025 ±0.002	-	-	-	-	-	-	-
Sinus	53.339 ±3.733	39.925 ±2.794	0.430 ±0.030	0.040 ±0.003	5.862 ±0.410	0.192 ±0.013	0.209 ±0.014	-	-	-	-	-	-	-	-	-	-
Tamol Sandoz	54.648 ±3.825	45.199 ±3.163	-	0.060 ±0.004	-	-	0.077 0.005	-	-	0.014 ±0.001	-	-	-	-	-	-	-
Vermi-don	53.918 ±3.774	45.835 ±0.065	-	-	0.118 ±0.008	-	0.113 ±0.008	-	-	0.014 ±0.001	-	-	-	-	-	-	-
Voltaren	18.461 ±1.292	23.354 ±1.634	0.359 ±0.025	1.406 ±0.074	53.040 ±3.712	0.520 ±0.036	-	2.847 ±0.199	0.009 ±0.001	-	-	-	-	-	-	-	-

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