Mini-review

Post-market surveillance of natural health products in Canada

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Abstract

Market trends indicate that natural health products are being used to maintain health as well as prevent and treat many medical conditions. A recent Canadian survey showed that 71% of the Canadian population have used a natural health product. Among these, many reports that they take natural health products on a daily basis. This review emphasizes on Canadian post-market surveillance system that apply to natural health products for human use. The public's perception is that the natural health products are all-natural, safe and effective, but there is still a wide variety of harms linked with these products. The post-market surveillance system is the monitoring window to observe and control the adverse effects of using natural health products. There are many activities involved in the post-surveillance to ensure the quality of the approved natural health products. Despite the fact that post-market surveillance plays a very important role in eliminating and/or reduce the risk of using natural health products, there are still some challenges and more work to be done to improve the outcome of the post-market surveillance of the natural health products.

Keywords: Adverse Reactions, Canada, natural health products, post-market surveillance, regulations

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Introduction

Over the last few decades, the market of Natural Health Products (NHPs) has numerously developed and expanded. The natural world is the main source of different vital nutrients that keep our bodies healthy. They contain either vitamin in a separate form such as vitamin C, or mixed with other vitamins such as vitamin A and E, or multivitamins. Also, they can contain minerals, amino acids, probiotics and remedies. They can be taken to restore and maintain health and to improve immunity and prevent many diseases. They can be called by different terms such as NHPs, "supplements," or alternative medicines [1]. The two most commonly used natural health products according to the survey are vitamins and other combination herbal, algal, and fungal products [2]. Canadian regulations apply to NHPs for human use and are categorized by substance and function. They specifically exclude biologics, substances regulated under the Tobacco act, controlled substances, prescription medications and products administered by injection.

The commercial sale of natural health products is subject to product and site licensing requirements of the NHPs and demonstrating compliance with the Canadian good manufacturing practices. Product license holders are required to monitor and report all serious adverse reactions. There are approximately 29,000 unauthorized NHPs currently available on the Canadian market. The majority of the manufacturers and importers of NHPs are cooperating to bring their products into compliance with the NHPs. Health Canada's approach for dealing with noncompliant NHPs is guided by a risk-based approach, as outlined by the Compliance Policy for NHPs.

The NHPs market in Canada

Natural Health Products can be obtained from many natural sources such as plants, marine and some micro-organisms. In some countries, NHPs have been known and used traditionally. There are more than 250,000 different kinds of plants, approximately half of them have been used for medicinal purposes. NHPs are getting more popular because of the perception that since they are natural, they are safer than taking pharmaceuticals. NHPs are offered on the market for many purposes, such as improving and promoting good health, preventive against various diseases, and enhancing lifestyle [2]. Health Canada has achieved some statistical studies demonstrate that 73% of Canadians use NHPs every day, monthly, or seasonally. The most common users are women, seniors, and people with some chronic medical conditions, for example, insomnia (sleeping difficulty), cancer, rheumatoid arthritis and others [3].

There are about 42,000 different NHPs in the Canadian market, and they are used for different applications [4]. Based on Statistics Canada, just in 2007 [5], the total retail sale of NHPs was $ 1.4 billion, the retail sale of the vitamins and supplements is about $ 865 million, followed by the remedies, sports nutrition and slimming products contributing $ 250 million, $ 110 million, and $ 145 million, respectively, as represented in **Figure 1**.

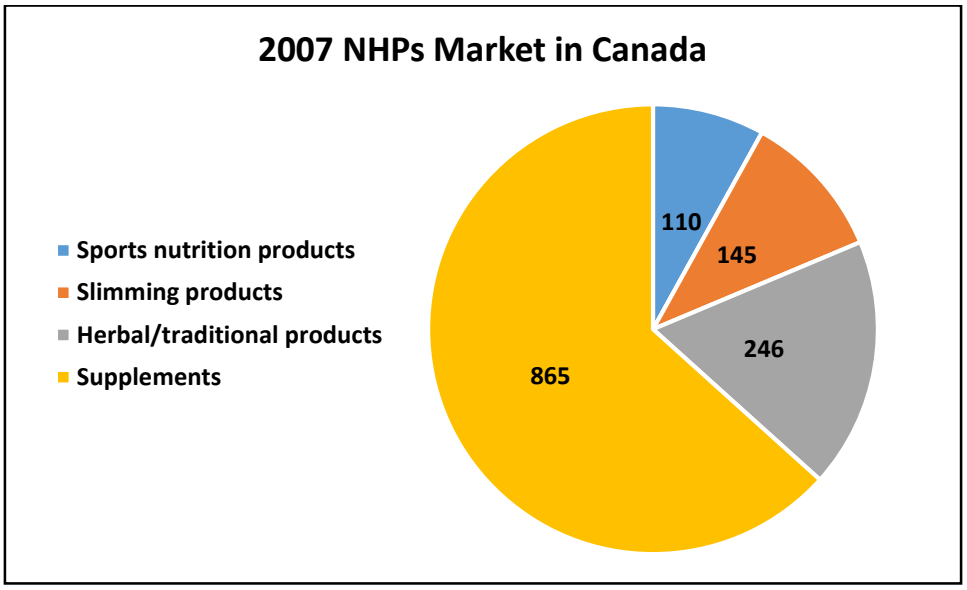

Figure 1: Natural Health Product market in Canada in million dollars

Post-market surveillance

Post-market surveillance is a significant process for follow-up, monitors and controls the safety of the NHPs after being authorized and approved by Health Canada to be sold in the Canadian market. It is very effective approach for tracking the adverse reactions (ARs) that can be produced by taking NHPs, verifying the important causal relationship between a NHP and medical condition and informing the public about if there is any safety concern [6]. The Canadian Institutes of Health Research defined post-market surveillance as post-market surveillance is the continued monitoring for, and the study of effects and other, safety and efficacy related aspects of, health products that have been marketed to the public [7]. According to Health Canada, post-market surveillance is essential in detecting and addressing safety issues and ensuring that a balance is maintained between the health benefits and the risks posed by all health products [8]. Each NHP can be extracted differently than the other. In other words, during the extraction procedure, different organic solvents can be used to extract the main substance, which can affect the chemical composition of each NHP, level of contamination, which may increase the risk to the public [9]. Also, the pharmacological and therapeutic actions of NHPs are not clear for some particular groups of the population, for example, children under 12 years old, pregnant women, older people and some patients who are already suffering from some chronic medical conditions. The lack of clear scientific evidence makes the clinical trials of NHPs more ambiguous, as they rely on their traditional use. When the

product is approved to be introduced in the market, then the post-market surveillance plays a significant role to estimate the benefit and harm of the approved products once they are launched in the market [10]. The main benefit of post-market surveillance can include an early warning for removal of the suspect product from the market resulting in increased user and patient safety, reduced litigation, providing feedback to research and development (R & D) groups to improve existing products, robust Quality Management System and greater regulatory standards compliance [11]. The post-market surveillance process needs a well-designed and structured methodological system. The surveillance tool relies on regulatory and scientific approaches. The regulatory process covers the approval of NHPs and the risk management plan that the manufacturers should submit. The scientific approach includes active communication between customers, manufacturers and health professionals. The post-market Surveillance can be classified into four different types as the following [12],

- Passive surveillance: Collecting data during this type of surveillance can be achieved by volunteer reporting, spontaneous reporting, or mandatory reporting.
- Active surveillance: Data can be collected by focusing on events, settings, or products of interest. Active surveillance is very effective in improving the number of reports with adverse reactions. In Canada, Sturdy of Natural health products Adverse Reactions (SONAR) is a pilot study that was conducted to improve the quantity of reported ARs linked to NHPs.
- Clinical Trials: are beneficial in understanding the mechanism of ARs, evaluation of post-market safety concerns and finding the best way to prevent it from occurring [13].

Monitoring the anticipated ARs of NHPs

The ARs can be observed when NHPs are taken, some can be seen immediately, such as skin rash, and other ARs can be seen after years of using the NHP, such as heart attack, kidney failure, liver cirrhosis and liver damage. Therefore, the usage of NHPs can be linked to some serious ARs and that might end with an urgent need for medical attention. Minniti-Ippolito and others [14] demonstrated that about 20 reported cases in Italy were suffering from severe ARs and about 16 reported cases of severe allergic responses linked to using Propolis. It is a bee derivative product used for treating some medical conditions such as dermatitis, ulcer and laryngitis. Some reported cases were admitted to the hospital, and two cases were reported as life-threatening cases. Researchers found that the label of two of those products was not warning the public of the anticipated ARs [15]. Taking NHPs with other prescription medication could cause some health risks, and unfortunately, this risk can be hidden because of the lack of monitoring by health care professionals. A Canadian study reported that about half the 140 surveyed physicians and pharmacists had noticed ARs in some patients already taking prescription medications and NHPs. Just two cases were reported to Health Canada [15].

Warnings and recalls of ARs of NHPs in Canada

In October 2006, Health Canada warned people about two unauthorized NHPs containing high levels of metals such as mercury and lead. The two products (Emperor's Tea and Hepatica extract) may include a high concentration of lead and mercury, leading to a very potential health risk, particularly for children under 12 years old and pregnant women. Poisoning by mercury or lead can cause very potential health risks such as anemia, uncontrolled blood pressure, organ damage (brain, liver and kidney) and can be life-threatening [15]. Russell [16] reviewed samples of NHPs from 25 different manufacturing sites in and outside Canada that Health Canada approves between 2017 and 2018. 13 sites were audited by inspectors from other countries to be approved in Canada, where 10 out of those 13 manufacturing sites showed a lack of evidence that the manufacturing lines were even inspected and reviewed. At the other 12 manufacturing sites, Health Canada did not verify types of evidence to prove the sites are following the required GMP guidelines, quality assurance or appropriate cleaning system. When reviewed about 75 licensed NHPs, including probiotics, it was found that 88% were introduced to the market using misleading information and about 56% with misleading label information. Some of these products do not have proven claims, including NHPs that should be relieving pain, fatigue and enhance burning fat [16].

In January 2008 [9], Health Canada announced warming to all Canadians not to use any of the NHPs produced by Manitoba Company Wild Vineyard because some of its products were contaminated with heavy metals such as lead. Because of the potential risks caused by taking these contaminated products, the manufacturing company was banned from all activities in Canada. The company recalled all its NHPs at the Canadian stores and online, although the company was not authorized to sell its products in the Canadian market [9]. This announcement

requested customers who used any product of Wild Vineyard and are concerned about this issue to contact their physician or pharmacist and report any ARs to Health Canada. Despite the intensive work and sophisticated approaches health Canada has been applying to monitor the NHPs during its life cycle, there is still more work should be done in order to protect the public health from hidden and undiscovered ARs. There are some recommendations for Health Canada to consider and they are as the following:

Coordination of the NHPs post-surveillance approach and all stakeholders: Improve the interaction and communication between the advisory committee members. Because of the significant role of the advisory committee in reviewing, evaluating, making an appropriate recommendation on NHPs for their safety and efficacy, it is important to increase the meetings of the advisory committee's members to discuss emerging NHPs events, share skills, and facilitate decision making on different NHPs events [17].

The ARs information centers of NHPs in Canada: The Poison Control Center (PCCs) should be used to report any ARs that can be seen as a result of using NHPs in the Canadian market. Involving the PCCs in the information gathering process can help post-market surveillance by directly reporting ARs and sharing information from the PCCs with Health Canada. It is also recommended that Health Canada should improve and establish links with all organizations involved in the NHPs field, to be able to share skills and knowledge about any ARs, and discuss and find solutions to overcome any anticipated harm to the society [18]. Globally, Health Canada should improve the level of communication with other international regulatory bodies such as MHRA in the UK, EMA in Europe, FDA, and Register of Chinese Herbal Medicine (RCHM) to collect and gather any ARs.

Reporting ARs to Health professionals: informing the medical care professionals about any ARs of NHPs is very important. In Canada, there is an online source center called Med-Effect to educate stakeholders generally about ARs of NHPs; however, providing the health care professionals with a period ARs reports would be more effective to update them about any ARs and to strengthen the ARs reporting system [17, 18]. It has been indicated that there is a lack of clearly set standards and communication guidelines between patients, physicians, and pharmacists [19].

Risk Management Plans (RMP): Health Canada should strengthen the surveillance of NHPs by implementing some rules and measures to assess, evaluate and minimize any anticipated risk. Establishing a solid Risk Management Plan (RMP) and issuing periodic reports should improve the level of communication, reduce risk, and provide better information about balancing between the benefits and risks of NHPs. Communicate with the manufacturers of NHPs, advisory committee members, health care professionals to build up a particular strategy and policy for establishing Risk Management Plans and providing clear reports periodically to at least some NHPs with a high-risk profile [20].

The Electronic Health Record (EHR): The quantity and quality of ARs reports are very significant, and linking all related information centers to gather data about each NHPs in the market should help health Canada obtain ARs reports. For instance, bridging between the Electronic Health Record (EHR) with health care professionals, other Canadian reporting systems can improve the quality of ARs reports. Involving physicians and pharmacists as experts to follow-up with patients' profiles individually to investigate any anticipated ARs, drug-diseases interaction, drug-drug interactions, or drug-food interactions [20].

Accessibility to NHPs: NHPs are widely distributed and sold through different places without direct monitoring by pharmacists and physicians. For instance, the stores for health and food products are considered the main channel for selling NHPS in the Canadian market. Many ARs cannot be monitored; some anticipated risks of taking NHPs while taking other medications can be life-threatening. For this reason, educating the public about the fact taking NHPs without health care professional advice can be harmful. These activities can be performed through the media, meetings, campaigns and other tools.

Ethical issues

Including plagiarism, Informed Consent, data fabrication or falsification and double publication or submission have completely been observed by the author.

Conflict of interest

The author has declared no competing interest.

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