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SHORT COMMUNICATION

Formulation and optimization of potassium iodide tablets

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Abstract The use of potassium iodide (KI) as a protective agent against accidental radioactive exposure is well established. In this study, we aimed to prepare a KI tablet formulation using a direct compression method. We utilized Design of Experiment (DoE)/mixture design to define the best formulation with predetermined physical qualities as to its dissolution, hardness, assay, disintegration, and angle of repose. Based on the results from the DoE, the formulation had the following components (%w/w): Avicel 48.70%, silicon dioxide 0.27%, stearic acid (1.00%), magnesium stearate 2.45%, and dicalcium phosphate 18.69%, in addition to potassium iodide 28.89% (130 mg/tablet). This formulation was scaled-up using two tablet presses, a single-punch press and a rotary mini tablet press. The final scaled-up formulation was subjected to a variety of quality control tests, including photo-stability testing. The results indicate that potassium iodide tablets prepared by a rotary mini tablet press had good pharmaceutical characteristics and a shelf-life of 25 days when stored at room temperature protected from light.

1. Introduction

As a trace element iodine is essential for the proper functioning of the thyroid gland as well as for other bodily normal metabolic functions. Goiter development is often associated with iodine deficiency. (Hendler, 2001) The thyroid gland preferentially absorbs iodine in its reduced form iodide. Inside the thyroid gland, iodine gets converted to triiodothyronine (T_3) and thyroxine (T_4) which are released into the systemic circulation for other bodily functions (Hendler, 2001; http://books.nap.edu/openbook.php?record_id=10868&page=R1). Iodide supplements, such as potassium iodide (KI), are available as iodide replenishing agents. Potassium iodide in particular may be used as an expectorant medication, to overcome a hyperactive thyroid, and systemically as an anti-fungal agent (Hendler, 2001; http://en.wikipedia.org/wiki/Potassium_iodide; http://www.drugs.com/mtm/potassium-iodide.html). Perhaps one of the main uses of KI is as a protectant against harmful radiation effects such as the one released in the air after a radioactive nuclear plant accident (FDA, 2002). Under these situations, radioactive iodine may

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be released to the environment surrounding the nuclear plant facility, and people living in the vicinity of the plant may be subject to dangerous radioactive exposure. The presence of radioactive iodine (^{131}I) in the thyroid gland may lead to the development of thyroid cancer. If taken during such emergencies, KI can saturate the thyroid tissues with iodine, preventing the accumulation of the radioactive form in these tissues (Hendler, 2001; http://books.nap.edu/openbook.php?record_id=10868&page= R1; FDA, 2002). Nuclear plant accidents, such as the ones occurred in April 1986 in Chernobyl (Ukraine) and more recently at the Fukushima Daiichi facility in Japan (2011), have prompted the authorities to consider the use of KI as a protective agent. For example, during the Chernobyl nuclear accident in the former Soviet Union, the authorities there distributed approximately 18 million doses of KI to the public following the incident, and studies since then revealed the absence of thyroid cancer in people who were treated with KI (http://en.wikipedia.org/wiki/Potassium_iodide; FDA, 2001, 2002).

In the *Federal Register* of December 15, 1978, the US Food and Drug Administration (FDA) declared that KI is a safe and effective measure to be taken during nuclear disasters. And, in the *Federal Register* of June 29, 1982, the FDA affirmed its earlier recommendation of administrating KI to the general public during nuclear incidents. In the United States, the FDA has approved several KI products since 2005 (Iosat, ThyroSafe, and ThyroShield). The FDA recommended a daily dose of 130 mg for adults and half that amount for anyone who is 18 years old or younger (FDA, 2001, 2003) To be effective, the dose should be given shortly before, immediately, or within four hours after the radio-iodine exposure. The FDA emphasizes the fact that administering KI is only one measure to be taken among others (seeking shelter, evacuation, etc.) during such emergencies (FDA, 2001, 2002, 2004).

The preparation of KI tablets may be achieved by a direct compression method. In this method, a dry blend of powders composed of active ingredients and fillers is prepared and then compressed as is on a tablet press without any added manipulations. Although this method is limited to only a few drugs, it is in particular suitable for potassium salts, such as KI (Shangraw, 1989; Armstrong, 2007; Shrewsbury, 2008). This method suffers from some disadvantages such as the build-up of static charge due to the dry nature of the powders being used and stratification within the granulation due to differences in the particle size and bulk density of the ingredients within a blend (Banker, 1991). However, several advantages to the method are recognized such as the absence of moisture and heat, less processing time, and fewer manufacturing equipment, among others (Shangraw, 1989; Armstrong, 2007; Banker, 1991).

The objective of this study was to formulate a tablet dosage form for potassium iodide using a direct compression method with the final aim of scaling-up the formulation to a finished dosage form.

2. Materials and methods

2.1. Materials

Potassium iodide was obtained from Acros Organics (Lot No. A0270423, NJ, USA). The other ingredients were purchased from their specified companies as follows: Dicalcium phosphate (JRS Pharma, Lot No. 7050X, Rosenberg, Germany), Avicel (FMC Corporation, Lot No. M218C, Philadelphia, PA), silicon dioxide (Cabot Corporation, Lot No. 1E128, Tuscola, IL), stearic acid (Fisher Scientific, Lot No. 880352, Fairlawn, NJ), and magnesium stearate (Spectrum Chemicals, Lot No. UJ0399, New Brunswick, NJ).

2.2. Methods

2.2.1. Design of experiment (DoE)/mixture design

We conducted a DoE/mixture design with 15 runs (Table 1). The design specifications are summarized in Table 2. The purpose of this design was to find the best composition that met the requirement in Table 2 (Section 2.A.). JMP Statistical Discovery Software (V. 10.0) (SAS Institute, Cary, North Carolina)/Design of Experiment facility was used in constructing the design and analyzing the data. The lower and upper limits of the ingredients listed in Table 2 (Section 2.B.) were determined from a reference handbook for pharmaceutical excipients (Rowe et al., 2006). Tests specifications followed USP guidelines as outlined in the subsequent sections.

Table 1 Mixture design table.

Run	Avicel	Silicon dioxide	Stearic acid	Magnesium stearate	Dicalcium phosphate	Dissolution	Hardness (kilopond)	Assay (mg)	Disintegration (min)	Angle of repose (°)
1	0.5	0.005	0.03	0.05	0.415	.	.	.	.	.
2	0.5	0.005	0.01	0.0025	0.4825	.	.	.	.	.
3	0.2	0.005	0.01	0.05	0.735	.	.	.	.	.
4	0.5	0.001	0.01	0.0025	0.4865	.	.	.	.	.
5	0.2	0.001	0.01	0.0025	0.7865	.	.	.	.	.
6	0.5	0.001	0.03	0.05	0.419	.	.	.	.	.
7	0.2	0.005	0.03	0.0025	0.7625	.	.	.	.	.
8	0.2	0.001	0.03	0.0025	0.7665	.	.	.	.	.
9	0.5	0.005	0.03	0.05	0.415	.	.	.	.	.
10	0.2	0.005	0.01	0.05	0.735	.	.	.	.	.
11	0.5	0.005	0.01	0.0025	0.4825	.	.	.	.	.
12	0.5	0.001	0.01	0.05	0.439	.	.	.	.	.
13	0.5	0.001	0.03	0.0025	0.4665	.	.	.	.	.
14	0.2	0.001	0.01	0.05	0.739	.	.	.	.	.
15	0.2	0.001	0.03	0.05	0.719	.	.	.	.	.