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# Optimisation of polymer coating process for microencapsulating ferrous fumarate for salt double fortification with iodine and iron

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**Abstract**
An extrusion-based encapsulation process has been developed for making salt grain-sized iron premix for salt fortification. The first step of extrusion agglomeration process has been studied and reported previously. The focus of this study is on the optimisation of the colour-masking and polymer coating steps. Several colour-masking techniques and polymer encapsulants were investigated at various encapsulation levels. Salt samples prepared by blending the resulting iron premixes with iodised salt retained more than 90% of the original iodine and more than 93% of the ferrous iron after 3 months storage at 35°C and 60% relative humidity (RH). Hydrophilic coatings such as hydroxypropyl methyl cellulose (HPMC) offered more protection at the 10% encapsulation level compared to other coating materials studied. All iron premix formulations exhibited high particle density, good bioavailability and acceptable organoleptic properties. The process using the most effective formulations and optimised operation parameters is ready for pilot scale testing and field studies.

**Keywords:** microencapsulation, hydrophilic polymer coatings, ferrous fumarate, salt double fortification

## Introduction

For the past 12 years, the food engineering research group at University of Toronto has been developing appropriate technology for the double fortification of salt with iodine and iron. This work is proceeding with the active scientific and financial support of the Micronutrient Initiative (MI) in view of its proven application to simultaneously address iron and iodine deficiency disorders, which together affect more than one-third of the world's population. The technology is based on physical separation of iodine and iron by microencapsulating iron in a concentrated premix which can be added to iodised salt to form double-fortified salt (DFS). A two-step encapsulation process was first developed based on iron particle agglomeration followed by lipid material coating using Würster-type fluidised bed equipment (Diosady, 2007 – Canadian Patent 2238925). This process has been scaled up to commercial production level and field tested for product stability and consumer acceptability (Diosady et al., 2004; Oshinowo et al., 2004, 2007). Clinical studies of DFS using the iron premix produced locally in India have proven that DFS is a simple yet powerful intervention in alleviating iron and iodine deficiencies simultaneously (Andersson et al., 2008).

In an effort to simplify the original fluidised bed-based agglomeration and encapsulation process, and to further improve the physical and chemical properties of the iron premix, a novel extrusion-based process has been developed more recently by our group. The process consists of extrusion, colour-masking and surface encapsulation (Figure 1); hence, this study has been carried out in several phases. The screening of compatible materials and feasible operation parameters has been reported previously (Li et al., 2010). Based on the understanding of the

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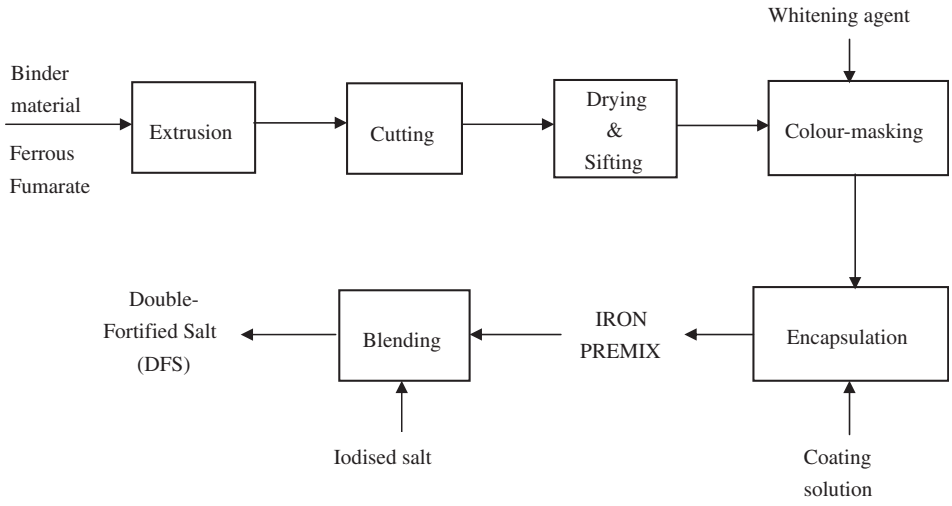


Figure 1. Schematic process flow for making microencapsulated ferrous fumarate.

Table 1. HPMC-based encapsulants used in this study.

| Encapsulant and supplier | Composition | Comments |
|---|---|---|
| Methocel E LV Premium series (Dow Chemicals, Midland, MI) | HPMC | The series consist of polymers with the same substitution ratios, but vary in viscosity. E3, E5 and E15 were investigated in the study. |
| Opadry White (Colorcon, West Point, PA) | HPMC, polyethylene glycol (plasticiser), talc (anti-tacking agent), and titanium dioxide (colourant) | This coating blend is a one-step system that incorporates the film-forming agent and additives all in one dry concentrate, making the coating process faster. |
| Sepifilm LP770 (Seppic, Castres Cedex, France) | HPMC, stearic acid (plasticiser), microcrystalline cellulose (binder) and titanium dioxide (colourant) | Sepifilm is a commercial, ready-to-use coating formulation that is soluble in the gastric juice and is widely used to coat moisture-sensitive particles. |

chemistry mechanism of iron–iodine interaction in DFS, we further optimised the extrusion agglomeration process (Li et al., 2011) and the ensuing coating steps. This article is focused on the development and optimisation of colour-masking and encapsulation processes.

Ferrous fumarate has been selected as the iron source, since it is readily bioavailable and has a bland taste, which makes it a good choice for iron fortification in foods. Unfortunately, it has a dark reddish brown colour which makes it conspicuous in the white salt. Thus, a colour-masking process is required to ensure the consumer acceptability of DFS containing the iron premix. Accordingly, several application techniques of titanium dioxide ($TiO_2$), an approved food-grade white pigment, were investigated in this study.

The final step of the iron premix production is microencapsulation, where the colour-masked particles are coated with a hydrophilic or hydrophobic polymer. This surface coating step has two functions: (1) the coating film serves as an extra physical barrier to protect the iron in the core of the premix and thus reduce the known interaction between iron and iodine and (2) it keeps the colour-masking layer in place ensuring the acceptable appearance of the final product.

Previously, hydrophobic coating materials, such as soy stearine (a fully hydrogenated vegetable oil), have been tested for encapsulating iron premix. The coatings gave acceptable iron stability and colour of the premix. However, the lipid material has poor film-forming capacity, resulting in particles with low density and not readily dissolving in a simulated gastric fluid solution (pH 1 HCl solution) (Li et al., 2009), indicating somewhat reduced iron *in vitro* bioavailability. Therefore, alternate coating materials were investigated in this study.

Hydrophilic coating materials have been widely used in oral drug delivery systems and can provide excellent physical barriers in the dehydrated, glassy state. Upon water penetration, they can achieve controlled release of the core ingredients by a swelling mechanism (Pham & Lee, 1994; Al-Tabakha, 2010). Many hydrophilic polymers used in pharmaceutical film coating processes are based on hydroxypropyl methylcellulose (HPMC). The HPMC-based encapsulants chosen in this study along with their compositions are presented in Table 1.

In addition to HPMC, polyvinyl alcohol (PVA)-based polymers are commonly used in applications that require immediate release characteristics. The main advantage of PVA systems is the enhanced moisture protection

properties (Siepmann et al., 2008). Several commercial PVA-based ready-to-use coating systems were investigated in this study.

Reverse-enteric coatings were also tested. These coatings are hydrophobic at pH > 6.5 and are hydrophilic at the gastric pH (<3), which can potentially provide a good moisture barrier to the coated iron premix without hindering the gastric acid dissolution profile (Kwon, 2005).

The objective of this study was then to identify the most suitable coating polymers and to optimise the microencapsulation process for producing desirable iron premix with high density, high bioavailability, improved appearance and colour, uniform size and shape and minimised reactivity when added into iodised salt.

## Materials and methods

Three groups of HPMC-based coating materials were tested in this study (Table 1), which are pharmaceutical grade polymers or polymer coating blends and were obtained from Dow Chemicals Co. (Midland, MI), Colorcon Inc. (West Point, PA) and Seppic Inc. (Castres Cedex, France), respectively. Kollicoat™ IR White from BASF Chemicals (Tarrytown, NJ) and Opadry™ AMB from Colorcon Inc. are PVA-based ready-to-use coating systems that were investigated in this study. Eudragit® E series produced by Degussa Rohm Pharma Inc. (Piscataway, NJ) consisting of cationic copolymers based on dimethylaminoethyl methacrylate and neutral methacrylic esters, and another enteric polymer, Aquacoat™ ECD produced by FMC Biopolymer (Newark, DE) were also investigated.

The other formulation components used were of food-grade. PAM™ olive oil spray and durum semolina were procured from local markets. Ferrous fumarate, particle size ~50 μm, was obtained from Dr Paul Lohmann Chemicals (Emmerthal, Germany). The whitening agent, $TiO_2$, was obtained from J. T. Baker (Stratford, Prince Edward Island, Canada). Food-grade, iodised salt (0.01% $I_2$ from potassium iodate) was provided by Kensalt, Kenya through the MI. The analytical reagents used for iodine and iron analyses were obtained from Sigma–Aldrich (Oakville, Ontario, Canada) at ACS analytical grade.

As reported previously (Li et al., 2011), durum wheat flour and durum semolina were better than rice and regular wheat flour as binder materials for making salt grain-sized iron particles by extrusion. They resulted in higher extrusion flow rates and better particle properties such as density and surface morphology. Thus, one of the best binder materials, durum semolina, was used in this part of the study for making extruded iron particles, which were used as the starting materials for investigation of colour-masking and polymer-coating processes. The detailed procedure for extrusion agglomeration was reported in Li et al. (2011).

Table 2. Optimised operation parameters for the fluidised bed coating.

| | |
|---|---|
| Temperature of process/fluidising air | 65–75°C |
| Fluidising air flow rate | 35–45% of the full flap opening |
| Flow rate of coating solution | ~1.5 mL/min |
| Nozzle air pressure | 1.8–2.2 bar |
| Vertical position of nozzle | 30 cm above the bottom of the chamber |

### *Colour-masking method*

The agglomerated iron particles made by extrusion were placed in a glass beaker and 25% (w/w) of titanium dioxide ($TiO_2$) powder was then added. A plastic spatula was used to manually blend the particles and the whitener powder for 10 min until the particles were uniformly coated and bright white in colour. A typical 200 g batch was prepared for the subsequent polymer-coating process.

### *Polymer-coating method*

A Uni-Glatt (Glatt Air Techniques, Ramsey, NJ) top-spray fluidised bed apparatus was used to coat the colour-masked iron particles with different polymer coating materials. The fluidised bed operation was a multi-step process that started with the polymer solution preparation. Depending on the formulation, a polymer powder was mixed with an ethanol:water solution (5:5, 6:4 or 8:2 ratio depending on the polymer used) and stirred continuously until the polymer was completely dissolved. Then, the colour-masked particles were placed in the fluidised bed chamber and were allowed to fluidise and warm up to 60–80°C in the machine for 10 min. After pre-warming the particles, the prepared coating solution was fed through the inlet tube by a peristaltic pump and sprayed onto the fluidised particles. The volume of the coating solution used for each batch varied depending on the coating solution concentration and the targeted coating level, e.g. 10% or 20% (dry weight basis, polymer/particles). The operation parameters such as air temperature and inlet solution flow rate were adjusted for each coating material used. The ranges for these variables are presented in Table 2.

### *DFS sample preparation and storage stability test*

The iron premixes prepared by the processes previously discussed were blended with the Kenyan iodised salt at a ratio of 1:150 to 1:200 to produce DFS with 1000 ppm iron. The DFS samples were packed in Zip-Lock™ polyethylene bags and stored at 35°C and 60% RH in a Precision™ Environmental Chamber (Precision Scientific, Chicago, IL) for 3 months. The storage condition was chosen to simulate the climatic conditions in many developing countries where iron and iodine deficiencies are of public significance. DFS samples were analysed for iodine and ferrous iron retentions initially and then monthly for 3 months.

*Iron premix property measurements*

The iron premix bulk density ($D_B$) and particle density ($D_P$) were determined by a modified procedure based on USP standard protocol ⟨616⟩, as reported in detail in Li et al. (2011). Iron content in the premixes was determined by spectrophotometry (Harvey et al., 1955; Diosady et al., 2002), as a complex with 1,10-phenanthroline. Iron dissolution rate in pH 1 HCl (the simulated gastric juice) was used as a close approximation of iron *in vitro* digestibility. The detailed procedure reported by Li et al. (2009) was followed, based on USP General Chapter ⟨711⟩ and Swain et al. (2003). Similarly, iron dissolution rate in a pH 4 HCl solution was used to assess the iron particle integrity, based on the fact that ferrous fumarate has relatively high solubility in the diluted acid, while the hydrophobic and lipid coating materials used in the study are not readily soluble at pH 4. This test is only applicable to coating materials that are insoluble at pH 4. Specifically, ~400 mg of the iron premix were dispersed in 1 L pH 4 HCl solution and the iron leached from the premix was measured by spectrophotometry. The iodine content of the DFS samples was determined by iodometric titration (AOAC method 33.149). The detailed procedure can be found in Diosady et al. (2002).

## Results and discussion

*Investigation of colour-masking variables*

Several techniques of applying $TiO_2$ to the extruded iron particles were investigated. Surface adhesion methods were explored by dusting the whitener powder on the extruded particles before drying and after drying, as well as with the aid of sprayed oil on the particle surface. The surface morphology of the particles prepared was then examined using a Hitachi Scanning Electron Microscope (Model S-2500, Tokyo, Japan). The SEM images are presented in Figure 2 for easy comparison. In all cases, 25% (w/w) of $TiO_2$ was used based on our earlier experience for proper coverage of the dark colour of the iron particles. After the samples of iron particles were coated, they were placed in the laboratory-scale fluidised bed machine at ~70°C for 10, 30 and 60 min to assess the effect of fluidisation on the adhesion of titanium dioxide. The temperature and time frame chosen were similar to the operating conditions normally used for fluidised bed microencapsulation in the laboratory.

In the dry adhesion process, the iron agglomerates were completely dried overnight at 50°C after extrusion to remove all moisture. The titanium dioxide adhered well to the particles (the SEM image on the far left in Figure 2) due to strong electrostatic forces (Ratanatriwong et al., 2003, Halim and Barringer, 2006). Even after 60 min of rigorous fluidisation, there was little change in the appearance (i.e. colour) of the particles, i.e. minimal loss of whitener layer.

In the wet adhesion technique, the extruded particles were coated immediately after extrusion. The particles contained approximately 12% moisture after extrusion and the moisture acted as the adhesive. The particles had a rough surface after wet coating and after 60 min of fluidisation, the titanium dioxide layer peeled off the surface like a layer of cracked paint, as shown in the SEM images in Figure 2 (two middle images). This is probably due to the drying which led to escape of moisture from the particles during the fluidisation (Cole et al., 1995; Fayed and Otten, 1997).

In surface oil adhesion method, the particles were lightly coated with a PAM™ olive oil spray in a laboratory rotating pan-coating apparatus soon after the extrusion. The particles were then dusted with titanium dioxide powder and allowed to tumble in the rotating pan until all the particles were evenly coated. The titanium dioxide adhered well before and after fluidisation (the SEM images on the far right in Figure 2), indicating that the whitener adheres well to oil. This was somehow expected and is in agreement with the literature indication that surface oil enhances powder adhesion, as seen in fingerprint techniques and salting of potato chips (Lee and Gaensslen, 2001; Buck and Barringer, 2007). The main problem with this method was that it was difficult to perform and the particles were likely to stick to each other in the pan-coating apparatus.

In summary, both dry adhesion and surface oil-aided adhesion worked well in terms of the appearance of colour-masked iron particles even after 60 min of rigorous fluidisation. The wet adhesion method did not work with

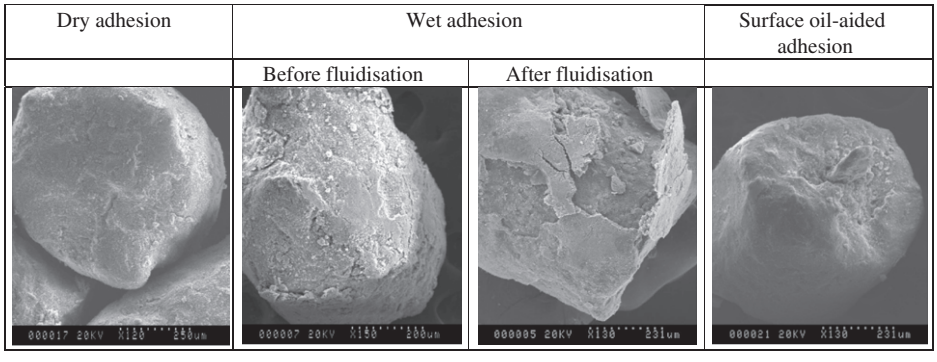


Figure 2. SEM images (~130× magnification) of iron particles prepared using three different colour-masking techniques.

fluidised bed coating, but might still work with other micro-encapsulation techniques such as pan coating. The technique chosen for the final formulation preparation was dry adhesion as it was easier to perform than the oil-aided surface coating.

### *Investigation of encapsulation variables*

During the preliminary investigation stage, several potential encapsulants were tested using the lab-scale fluidised bed machine. The key results from the preliminary investigation are presented in Table 3, indicating that the fluidised bed process could be used to successfully coat iron particles when using appropriate polymer materials and under proper operation parameters (Fayed and Otten, 1997; Dewettinck and Huyghebaert, 1999). Six polymer coating materials were then selected for further study and compared with soy stearine (Diosady et al., 2004).

Next the coating formulation variables were optimised, including the proper solvent, and co-solvent if necessary, solvent to co-solvent ratio, and the polymer concentration in the coating solutions. These parameters varied depending on the type of polymer and other additives present in the commercial coating blends. The optimised coating solutions containing the selected polymers at various concentrations are presented in Table 4. The combination of optimal formulation variables was aimed to ensure the viscosity of the coating solutions that was within a desirable range of 2.5–3 mPa s, which is recommended by the literature for fluidised bed coating operations (McGinity, 1997; Dow Chemical, 2002 – Methocel™ User Manual). Although most of the polymer coatings were designed to be used in aqueous solutions, water–ethanol mixed solvent systems were used in this study since the polymers tended to agglomerate when sprayed in solely aqueous solutions. A possible explanation for this phenomenon is related to the insufficient capability of the lab-scale fluidised bed machine (a relatively old model) to rapidly evaporate all the water from the coating solution, leading to wet particles sticking together. The introduction of ethanol into the spraying solution system (as shown in Table 4 with optimised co-solvent formulations) resulted in quicker evaporation of the solvents, so as to avoid the potential particle agglomeration during the surface coating process (Cole et al., 1995; Guignon et al., 2002; Ghosh, 2006). An ongoing field test with two pharmaceutical companies in India under the sponsorship of MI has shown polymer coating solutions prepared by aqueous only solvent (water) can achieve equally desirable quality of coated premix when using pilot- or commercial-scale fluidised bed processors/coaters.

Table 3. Preliminary investigation results on encapsulant feasibility.

| Encapsulant (commercial name) | Polymer chemical form | Observations/comments |
|---|---|---|
| Methocel E3 | HPMC polymers | • Uniform coating and easy to use<br>• *Not used* in final formulations because coatings with Methocel E6 were stronger. |
| Methocel E6 | | • Uniform coating which could withstand abrasion<br>• *Used* in final formulations |
| Methocel E15 | | • Solution viscosity was too high to perform coating<br>• *Not used* for further trials |
| Opadry white (contains colourant, $TiO_2$) | HPMC-based, ready-to-use coating blends | • Uniform coating<br>• The coated iron premix appeared bright white due to titanium dioxide present in this commercial coating blend<br>• *Highly recommended and used* in final formulations |
| Opadry II white (contains colourant, $TiO_2$) | | • Coating layer was rough and uneven<br>• *Not used* in final formulations |
| Sepifilm LP770 (contains colourant, $TiO_2$) | | • Strong, uniform coating layer with few defects<br>• Particles were bright white due to titanium dioxide included in the commercial blend<br>• *Highly recommended and used* in final formulations |
| Kollicoat IR white (contains colourant, $TiO_2$) | PVA-based, ready-to-use coating blends | • Weak, flaky coating layer formed, which also easily came off when iron particles were blended in salt.<br>• *Not used* in final formulations |
| Opadry AMB (contains colourant, $TiO_2$) | | • Uniform coating with some minor defects<br>• Strong film<br>• *Recommended and used* in final formulations |
| Eudragit EPO | Reverse-enteric coating polymer | • Uniform, glossy coating that was resistant to abrasion<br>• *Recommended and used* in final formulations |
| Aquacoat ECD | Enteric coating polymer | • Moderately uniform coating<br>• *Recommended and used* in final formulations |
| Soy stearine | Hydrogenated soy bean oil, lipid coating material | • Coating formulation was based on previous studies (Diosady et al., 2004 and 2007).<br>• Uniform, smooth coating<br>• *Used* in final formulations as a control/comparison |

Table 4. Optimised coating solution variables when used in final formulation preparation.

| Polymer | Solvent/co-solvent solution | Polymer concentration in coating solution (% w/v) giving desired viscosity for coating to proceed in the lab-scale fluidised bed processor (the desired viscosity was pre-determined at ~3 mPa s) |
|---|---|---|
| Methocel E6 (HPMC) | 60:40 (ethanol:water) | 2.5% |
| Opadry white (HPMC-based) | 60:40 (ethanol:water) | 4% |
| Sepifilm LP770 (HPMC-based) | 60:40 (ethanol:water) | 3% |
| Opadry AMB (PVA-based) | 50:50 (ethanol:water) | 6% |
| Eudragit EPO (Reverse enteric) | 80:20 (ethanol:water) | 3% |
| Aquacoat ECD (enteric coating) | This commercial coating is already available as a liquid dispersion | 5% |
| Soy stearine (lipid material) | 60:40 (ethanol:water) | 5% |



*Effect of polymer coatings on iron premix properties*

As stated earlier, the extruded iron particles made with durum semolina and a binder-to-ferrous fumarate ratio of 20:80 were used as the starting material for investigation of colour-masking and polymer coating processes. $TiO_2$ was used at 25% (w/w) as the optimal whitener. Since some commercial coating materials already included $TiO_2$, with these coating materials the extra $TiO_2$ level was appropriately reduced.

For encapsulation, seven encapsulants identified from the preliminary study (Table 3) were tested at two coating levels, 10% (w/w) and 20% (w/w). During the preliminary investigation, 10% (w/w) coating was shown to be the minimum encapsulant level required to protect the iron from interacting with iodine in DFS (Li et al., 2010). The 20% (w/w) encapsulation level was chosen in an effort to determine whether or not a higher coating level enhanced the stability of the DFS product.

The agglomerated iron particles made with durum semolina had a particle density ($D_p$) of approximately 1.76 g/cm$^3$ (Li et al., 2011). When 25% of $TiO_2$ was applied to the extruded iron particles, the density increased to ~1.96 g/cm$^3$, due to the high density of titanium dioxide (4.4 g/cm$^3$). After encapsulation using various polymers, the particle density decreased somewhat to 1.67–1.68 g/cm$^3$ for 2.5% $TiO_2$-coated particles and to 1.77–1.85 g/cm$^3$ for 25% $TiO_2$-coated particles. This decrease can be attributed to the loss of $TiO_2$ caused by the strong upward air flow during the fluidised bed coating process. Nevertheless, all final iron premix particles had densities similar to iodised salt (1.86 g/cm$^3$), which should ensure a uniform distribution of iron in DFS.

The chemical properties of the iron premixes prepared using the optimised formulations are summarised in Table 5. All the iron premixes produced had >20% of total iron, with the highest iron content of 24% in Formulation P-15 made by 20% of Opadry AMB coating. This is significantly higher than the iron content of the premix (14–15%) made by the previous fluidised bed agglomeration/coating process. This leads to lower premix requirement and reduced the cost of the final DFS product. In addition, over 93% of the encapsulated iron (Table 5, in all formulations P-1 to P-15) remained in the ferrous form, which suggested that the processing steps had little impact on ferrous fumarate oxidation and thus iron bioavailability. The polymer coatings actually contributed to ferrous iron retention as the coated samples had more ferrous iron after storage than uncoated extrudates (Li et al., 2010).

The acid dissolution tests were performed at two levels, pH 1 and pH 4, for the determination of iron *in vitro* bioavailability and particle integrity, respectively. As shown in Table 5, less than 10% of encapsulated iron was leached into the diluted HCl solution (pH 4) after 2 h, indicating that ferrous fumarate was well retained within the premix, due to the surface protection of the polymer coating. This is in agreement with the literature (McGinity and Felton, 2003; Bley et al., 2009; Al-Tabakha, 2010). During the simulated digestibility test, the majority of iron (>96%) in the premixes coated by hydrophilic polymers dissolved within a period of 2 h, suggesting that the iron premixes were able to release iron quickly under acidic conditions and were therefore likely to be highly bioavailable. This is not unexpected as the selected hydrophilic polymers have been used in many pharmaceutical applications to formulate drug delivery systems for targeted or controlled release (Nagai et al., 1997; Kamel et al., 2008; Al-Tabakha, 2010). Even with hydrophobic coatings, such as soy stearine, over 93% of iron could be released after 2 h, perhaps through the development of surface defects.

*DFS storage stability test*

The main reason for encapsulating iron before blending into iodised salt was to introduce a physical barrier to prevent the known reaction of iodine and iron which would lead to iodine loss from DFS. As stated earlier, seven different encapsulants were used to prepare 15 final iron premixes, which were added into the Kenyan iodised salt in forming DFS. The storage stability of DFS samples was followed over a period of 3 months at 35°C and 60% RH.

Figure 3 illustrates the effect of the encapsulants on the iodine retention in DFS when the polymer coatings were used at the 10% encapsulation level. There was no

Table 5. Iron content and dissolution rate of the iron premixes prepared using the optimised formulations.

| Premix number | Formulation variables | | | Total iron content in the premix right after premix preparation (%, wt) | Ferrous retained in the DFS after 3 months storage (%, ferrous vs. total iron) | % iron leached in pH 4 HCl solution after 2 h (indication of coating integrity) | % iron released in pH 1 HCl solution after 2 h (iron *in vitro* digestibility) |
|---|---|---|---|---|---|---|---|
| | Extrusion | Colour-masking | Microencapsulation | | | | |
| P-1 | Durum semolina and ferrous fumarate, based on a binder-to-iron ratio of 20:80 (dry weight) | $TiO_2$ 25% | Eudragit EPO 10% | 23.1 | 95.6 | 9.5 | 99.7 |
| P-2 | | | Eudragit EPO 20% | 21.9 | 96.3 | 7.6 | 98.9 |
| P-3 | | | Sepifilm 10% | 21.6 | 96.9 | 9.2 | 96.3 |
| P-4 | | | Sepifilm 20% | 22.0 | 96.0 | 7.5 | 97.4 |
| P-5 | | | Opadry 10% | 23.4 | 95.9 | 9.6 | 99.6 |
| P-6 | | | Opadry 20% | 22.4 | 96.1 | 8.3 | 98.2 |
| P-7 | | | Methocel E6 10% | 22.8 | 95.2 | 6.7 | 100.0 |
| P-8 | | | Opadry AMB 10% | 22.0 | 95.6 | 8.8 | 97.4 |
| P-9 | | | Opadry AMB 20% | 21.9 | 94.8 | 8.5 | 99.2 |
| P-10 | | | Aquacoat 10% | 23.1 | 95.1 | 8.1 | 97.4 |
| P-11 | | | Soy stearine 10% | 20.4 | 96.7 | 9.2 | 93.4 |
| P-12 | | | Soy stearine 20% | 19.8 | 96.3 | 7.6 | 95.2 |
| P-13 | | $TiO_2$ 2.5% | Sepifilm 20% | 23.4 | 94.6 | 6.0 | 98.1 |
| P-14 | | | Opadry 20% | 22.5 | 93.9 | 6.8 | 98.7 |
| P-15 | | | Opadry AMB 20% | 23.9 | 93.5 | 6.2 | 98.6 |

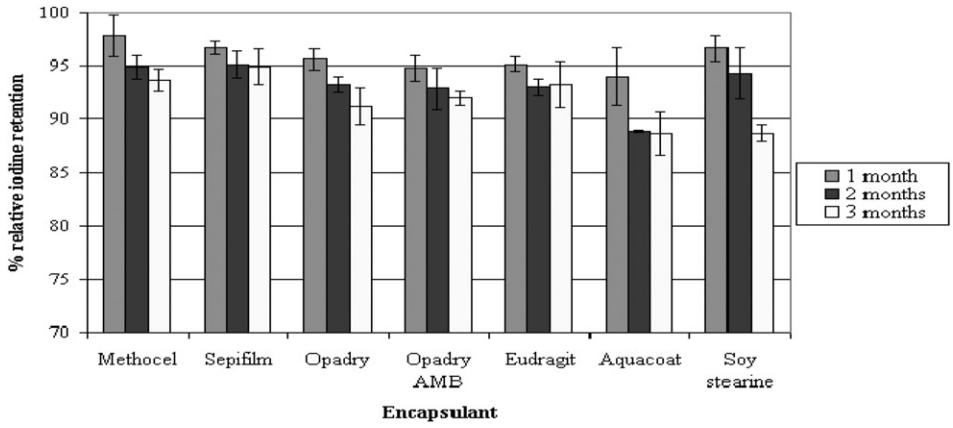


Figure 3. Effect of encapsulant type on the iodine retention in DFS (based on 25% $TiO_2$ colour-masking and 10% encapsulation level, data from samples P-1, P-3, P-5, P-7, P-8, P-10 and P-11) (error bars represent mean ± standard deviation, $n = 4$).

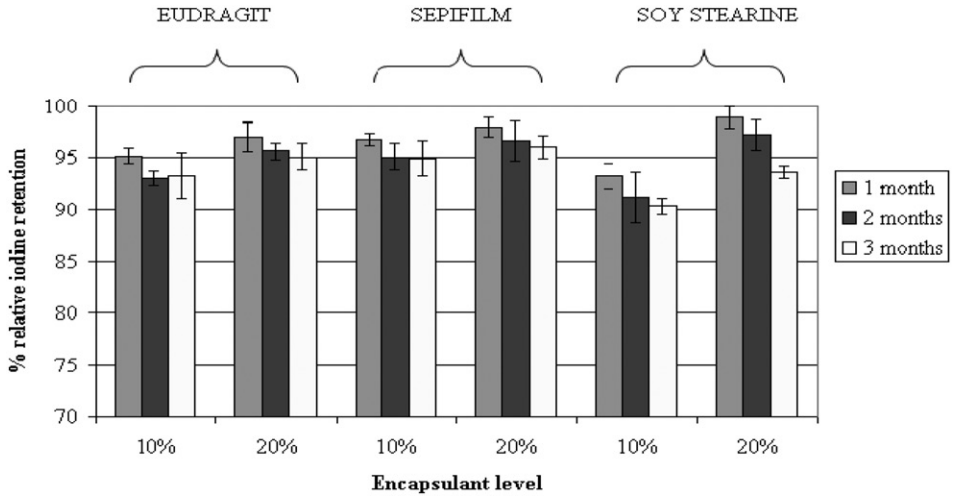


Figure 4. Effect of encapsulation level on the iodine retention in DFS (based on 25% $TiO_2$ colour-masking level, data from samples P-1 vs. P-2; P-3 vs. P-4; P-11 vs. P-12) (error bars represent mean ± standard deviation, $n = 4$).



significant difference between the encapsulants and most DFS samples were able to retain over 90% of iodine after 3 months. Methocel (Dow Chemicals) and Sepifilm LP770 exhibited slightly better iodine retention and were recommended for further pilot plant trials. The enteric coating, Aquacoat, and the hydrophobic coating, soy stearine, were not able to retain as much iodine as the hydrophilic coatings, suggesting that hydrophilic coatings offer more protection at lower encapsulation levels.

The encapsulation level has the expected effect on the relative iodine retention. A higher encapsulation level (20%) offered a better barrier between the iron and iodine. As seen in Figure 4, the premix samples prepared at the 20% encapsulant level significantly retained more iodine after 3 months storage at high temperature (35°C) and RH (60%).

The effect of different colour-masking levels is shown in Figure 5. The samples prepared at the 2.5% $TiO_2$ coating level retained less iodine after 3 months, compared to those prepared with 25% of titanium dioxide coating. This indicated that the colour-masking layer of titanium dioxide had a protection effect on iodine retention and acted as a physical barrier between the iron and iodine in the salt. This effect is more or less similar to its blocking effect in sunscreen skin lotion products (Diebold, 2003). Thus, reducing the titanium dioxide level is not advantageous.

## Conclusions

Extrusion of ferrous fumarate followed by $TiO_2$ colour-masking and polymer coating has been proven to be a technically feasible approach to manufacturing iron premix for double fortification of salt with iodine and iron. The new process for iron premix production has been successfully optimised and is ready for pilot-scale trials. Specifically, three colour-masking techniques and several polymer encapsulants were investigated at various encapsulation levels. The most suitable coating polymers

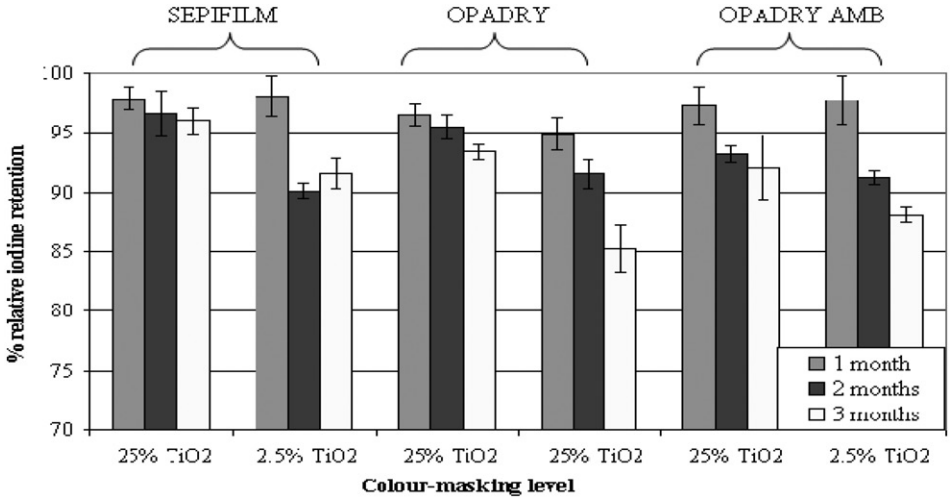


Figure 5. Effect of the colour-masking level on the iodine retention in DFS (based on 20% encapsulation level, data from samples P-4 vs. P-13; P-6 vs. P-14; P-9 vs. P-15) (error bars represent mean ± standard deviation, $n = 4$)

identified in the preliminary test were further studied to obtain optimised formulations and operation parameters for producing microencapsulated iron premix with desirable physico-chemical properties.

During the extrusion step, durum wheat flour and semolina were shown to be excellent binders for agglomerating ferrous fumarate powder into salt grain-sized microparticles (Li et al., 2011). In this study, $TiO_2$ used as the colour-masking agent adhered well to the completely dried, extruded iron particles through electrostatic binding, allowing a full coverage of the dark brownish colour of the iron compound. We found that Methocel E6 (sample P-7) and Sepifilm LP770 (samples P-3 and P-4) could form strong films on the surface of colour-masked iron particles that protect the ferrous iron in the premixes from interacting with the salt matrix or iodine. The iron premix formulations made by these HPMC-based polymers retained ~95% of the original ferrous iron, and ~95% of the original iodine in dry, refined iodised salt after 3 months storage at 35°C and 60% RH. The premixes had high bulk and particle densities, matching that of salt grains; high *in vitro* iron bioavailability; excellent particle integrity; and improved appearance and colour compared to the premix made by the previous technique of fluidised bed agglomeration/coating, thus meeting all objectives of this study.

In addition to the selection of appropriate coating polymers, proper encapsulation levels also presented positive effects on the quality of final products. While 10% encapsulation by hydrophilic polymers was adequate for preventing the iron–iodine interaction in DFS samples, 20% coating is preferred for mechanical integrity.

The approach reported here will likely reduce the cost and complexity of the process of iron premix production. Pilot tests with two pharmaceutical companies in India have been initiated. Further tests with unrefined, coarse salt with high moisture content and significant impurities will be used to explore the limitations of this technique. The success of the current development will provide improved cost-effective technology for addressing the most pressing nutritional deficiencies now effecting more than 2 billion people, primarily in the developing world.

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## Declaration of interest

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of this article.

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