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► To cite this version:

Xavier Rouau, Joel Abecassis, Cecile Barron, Marc Chaurand, Youna Hemery, et al.. Grain fractionation revised for new healthy ingredients. Cereal & Europe Spring Meeting - Whole Grain Global Summit, Mar 2009, Newcastle, United Kingdom. hal-01603373

HAL Id: hal-01603373

<https://hal.science/hal-01603373>

Submitted on 4 Jun 2020

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Cereal processes were long optimised for products containing only grain endosperm. So the milling technology has been improved over the centuries for the production of white flour or semolina as a major product exhibiting excellent functional and sanitary properties for second transformation. However, a large part of the bioactive compounds of the grain that are preferentially located in the outer layers is thus excluded from the mass cereal foods. The manufacture of whole grain products (or inclusion of whole bran in flours) constitutes a possible response to better exploit the grain nutritional potential but with some limitations. The breadmaking functionality of whole grain flours makes it difficult to manufacture diversified and appealing products for consumers. Also the outermost layers of the grains may contain some contaminants which are detrimental to the sanitary quality of the flours. At last, the bioactive compounds exhibit in general a poor availability as they are trapped in the cellular fibrous structures of the envelopes. Revising the conventional grain fractionation processes in considering the properties and potential of all its different parts and tissues will aim at producing new healthy functional ingredients for cereal-based food products of high sensory quality. New tools designed to gain a better understanding of grain tissue structure and their behaviour upon processing are necessary to develop and optimize a new grain fractionation technology. For example, the combination of milling and debranning monitored by a grain tissue marker methodology can allow to tailor flours with different levels of peripheral layers inclusion, quantitatively and qualitatively. The by-products from the milling industry (brans) can be exploited also as a source of healthy ingredients. They can undergo different cracking diagrams using advanced technologies of grinding and separation, to result in concentrates of grain tissues or sub-fractions of contrasted functional properties with improved availability of bioactives.